DETECT: DEfining the Target volume for Endoluminal radiation boosting in patients with reCTal cancer

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Primary objectiveTo determine the maximum distance of microscopic tumor spread per patient in all directions from the macroscopic tumor remnant in the pathology specimen.Main secondary objectives- To determine the maximum distance of microscopic…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Malignant and unspecified neoplasms gastrointestinal NEC
Study type	Observational invasive

Summary

ID

NL-OMON52208

Source
ToetsingOnline

Brief title
DETECT

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC
- Gastrointestinal neoplasms malignant and unspecified

Synonym
rectal cancer, rectal carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic
Source(s) of monetary or material Support: ZonMw (TZO),Wellicht de Faculty of Health,

Medicine and Life Sciences (UM) via het SCANNEXUS FHML scanning hours fund

Intervention

Keyword: Endoluminal radiation boosting, Microscopic tumor spread, Rectal cancer, Target volume definition

Outcome measures

Primary outcome

Maximum distance of microscopic tumor spread per patient in all directions:

The maximum distance of microscopic tumor spread in all directions from the macroscopic remnant in the specimen will be measured per patient in millimeters using a standardized protocol by the pathology department.

Secondary outcome

Main secondary parameters/endpoints

- Maximum distance of microscopic tumor spread per patient in all directions as seen by eye and/or on imaging (ultrasound, MRI):

A tissue deformation factor/model and the location of the microscopic tumor spread in relation to the macroscopic remnant determined during pathological analysis, will be used to determine the maximum distance of microscopic tumor spread as seen by eye and/or on imaging (US, MRI) per patient in all directions in millimeters.

- Treatment margin relative to the macroscopic tumor to cover 90% and 95% of MTS:

90% and 95% of the maximum distance of MTS in all directions in millimeters including 95% confidence intervals, both reported including and excluding ypT0 patients. Reported both by eye and on imaging, for which i.a. the tissue

deformation model will be used.

Study description

Background summary

To date, the backbone for treating non-metastatic rectal cancer is surgical resection of the rectum and the perirectal fat that surrounds it. Depending on gross tumor characteristics, patients may receive neoadjuvant radiotherapy or neoadjuvant concurrent chemoradiotherapy to reduce the locoregional recurrence rate. With the currently used neoadjuvant concurrent chemoradiation schedule a complete tumor response is achieved in 10-20% of all patients. In patients with a clinical complete response, omission of surgery with thorough follow-up (*watch and wait*) and salvage surgery at the time of local recurrence can be considered instead of surgery. Surgery related morbidity and side effects, like for example a colostomy, can then be avoided.
A very promising approach to increase the rate of complete responders while still preserving rectal function is to add an endoluminal radiation boost to the residual tumor in patients with limited residual disease after concurrent chemoradiotherapy. These endoluminal techniques allow for a more localized boost compared to external beam radiotherapy (EBRT), which enables radiation dose escalation to the tumor and limits the radiation induced toxicity. Various series have shown that endoluminal boosting results in high complete response rates (60-86%) and limited toxicity in selected patients.
Unfortunately, widespread introduction of endoluminal techniques is hampered by a lack of fundamental knowledge on the definition of the treatment volume. In order to achieve tumor control not only the macroscopic tumor, also known as the gross tumor volume (GTV), but also the microscopic tumor spread (MTS) needs to be treated. Crucial information regarding the treatment margins needed to cover this microscopic spread is currently lacking.
This project will for the first time provide hard data regarding MTS in all directions from the macroscopic tumor in pathology specimens, as seen by eye (endoscopically & rectoscopically) and on imaging (endo-ultrasound, MRI) of a prospective cohort of patients who undergo a surgical resection after neoadjuvant treatment for rectal cancer. These data will be used to develop evidence based guidelines for target volume definition in rectal endoluminal radiation boosting.
Such guidelines are essential to improve the quality of rectal endoluminal radiation boosting and to facilitate the widespread availability of the techniques. High quality endoluminal radiation boosting will increase the clinical complete response rates and allow omission of surgery in rectal cancer patients. Surgery related morbidity, such as a permanent colostomy can then be avoided.

Study objective

Primary objective
To determine the maximum distance of microscopic tumor spread per patient in all directions from the macroscopic tumor remnant in the pathology specimen.

Main secondary objectives
- To determine the maximum distance of microscopic tumor spread per patient in all directions from the macroscopic tumor remnant as seen by eye (endoscopically/rectoscopically) and/or on imaging (endo-ultrasound, MRI).
- To determine the treatment margin (in the various directions) relative to the macroscopic tumor to cover 90% and 95% of all microscopic tumor spread.

Study design

Prospective multicentre cohort trial in >=50 patients with a residual ycT1-3N0 tumor after neoadjuvant chemoradiotherapy or radiotherapy for rectal adenocarcinoma at least 6 weeks after the neoadjuvant treatment.

Study burden and risks

Patients will receive the same standard care that they would receive when not participating in a study: among others flexible endoscopy, MRI, surgery, pathological processing/analysis. In addition to this, they will undergo a rectoscopy and 3D endo-ultrasound before TME surgery. For Maastro and MUMC+ patients, the 3D endo-ultrasound and rectoscopy will be performed on the same day as the surgery, reducing the study burden for the patient, and under general anaesthesia, further reducing the burden for the patient. Application of general anaesthesia is part of standard care (part of TME surgery). For CZE patients, the endoscopy and endorectal ultrasound are part of standard care and both procedures will be performed a few days before TME surgery. Based on the results of the endoscopy, the physician will decide if an ultrasound will be performed or not for CZE patients. The rectoscopy and 3D-ultrasound bear a very limited safety risk. No follow-up visits related to the trial will be necessary.

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

- >=18 years of age and capable of giving informed consent.
- ycT1-3N0 residual histology confirmed rectal adenocarcinoma after neoadjuvant radiotherapy or long-course chemoradiotherapy for which patients will undergo TME surgery.
- Minimal interval between end of neoadjuvant chemoradiotherapy or radiotherapy: 6 weeks.

Exclusion criteria

- Patient has received brachytherapy as part of neoadjuvant treatment.
- <18 years of age or incapable of giving informed consent.
- Patient has not been treated with neoadjuvant radiotherapy or long-course chemoradiotherapy.
- Patient will not undergo TME surgery for a ycT1-3N0 residual histology confirmed rectal adenocarcinoma.
- Interval between end of neoadjuvant therapy and surgery is <6 weeks.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-11-2023
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	26-11-2021
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT04927897
CCMO	NL77886.068.21