Macroscopic and microscopic changes of a locally advanced rectal tumour during radiotherapy: assessment using anatomical, functional and cinematic MRI.

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

Summary

ID

NL-OMON39583

Source
ToetsingOnline

Brief title
Imaging in locally advanced rectal cancer.

Condition

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

Synonym
Colorectal carcinoma, rectal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Dosis escalation, Functional MRI, Locally advanced rectal cancer, Neo-adjuvant radiochemotherapy

Outcome measures

Primary outcome

Observational study to analyse rectal tumour regression and tumour movement

during long course pre-operative RCT for LARC in order to develop a dose

escalation strategy for rectal cancer. Besides this first endpoint it is also

an explorative study to analyse the feasibility to apply anatomical and

functional MRI during RCT in the evaluation of treatment response.

Secondary outcome

Not applicable.

Study description

Background summary

The standard of care for locally advanced rectal cancer (LARC) is 5 weeks neo-adjuvant radiochemotherapy (RCT) followed by radical surgery 6-8 weeks afterwards. Surgery is performed independent the response to RCT and is attended with substantial morbidity such as the need for colostomy, faecal incontinence, urinary incontinence, perineal pain and impaired bowel function or sexuality.
A pathological complete response (pCR) rate ranging from 12-24 % is reported after neo-adjuvant irradiation combined with capecitabine chemotherapy. This response rate is dose dependent. The higher the delivered radiotherapy dose the better the tumour response. Dose escalation therefore is attractive but unfortunately limited because of toxicity due to irradiation of surrounding healthy tissues.

Two dose escalation strategies are possible, sequential boost after completion of elective field irradiation and boost dose delivery during irradiation of the elective field. Safe dose escalation is only achievable when there are little to no healthy tissues in the boost field but still assurance of full tumour coverage. For boost field delivery during radiotherapy adaptation of the boost field is needed to tumour shrinkage and tumour movement during therapy. For sequential boost delivery adaptation is needed to tumour shrinkage and movement during the week after RCT.
Development of a safe dose escalation strategy and so optimizing tumour response is correlated with clinical outcome and could also be important in medical decision making. A few retrospective studies compared clinical outcomes in patients with clinical complete response (cCR) without surgery to clinical outcomes in operated patients with pCR to RCT. The similar outcomes found in these studies indicate the possibility to perform RCT as sole treatment in patients with a good response. This approach is of obvious interest, but unfortunately remains controversial because of the known dissociation between clinically and pathologically assessed response.
To discriminate patients with a good response from patients with a poor response to RCT, a reliable tool is needed. Anatomical MRI, which is an accurate imaging modality for staging of LARC, has a low accuracy after RCT because of improper discrimination between fibrosis and vital tumour. Functional MRI imaging shows promising results in tissue discrimination because it reflects tissue function and microanatomy, therefore it could be a more reliable option for pathological response prediction.
With the combination of both tumour shrinkage and movement information during therapy and reliable tumour pathological response prediction methods a first step is made to safe dose escalation which leads to better response to RCT and the possibility of personalised multimodality treatment in the heterogenic group of LARC.

Study objective

The purpose of this pilot study is twofold:
- evaluation of the tumour movement and regression during and short after long course pre-operative therapy for locally advanced rectal cancer in order to develop an integrated or sequential dose escalation strategy for rectal cancer;
- examination of feasibility to use repeated functional MRI imaging during pre-operative treatment to predict pathological response after surgery.
With the combination of this knowledge a first step is made to safe dose escalation which results in better response and the possibility of personalised multimodality treatment in the heterogenic group of locally advanced rectal tumours.

Study design

Prospective pilot study with weekly MRI during long course pre-operative RCT

and one MRI during the second week after RCT for LARC. The MRI protocol consists of anatomical and cinematic MRI for assessment of movement characteristics and tumour shrinkage and functional MRI for tumour response assessment. The clinical tumour response will be correlated with pathological tumour regression grade.

Study burden and risks

For study purposes patients will undergo six extra MRI scans. After proper screening the use of MRI is free of any risks. Five scans will be scheduled in combination with radiation treatment and one scan will be scheduled in the second week after RCT. For this last scan patients will receive reimbursement of travelling expenses.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3584 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Rectal tumor < 15 cm anal verge
- Biopsy proven adenocarcinoma
- cT3-4 N0-2 M0: based on standard primary staging

Exclusion criteria

- Patients who meet exclusion criteria for MRI at 3T
- Patients with inflammable bowel disease or diverticulitis
- Patients with history of pelvic surgery
- Patients with history of pelvic tumours

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-04-2011
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO

Date:	20-05-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Approved WMO Date:	29-12-2014
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	NL31131.041.10