Organ motion and early tumor response measurement during chemoradiotherapy for esophageal cancer.

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To quantify motion based variation of the target volume of the primary tumor over the course of chemoradiotherapy in esophageal cancer patient, and to use this information to calculate appropriate PTV (planning target volume) margins according to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON44849

Source
ToetsingOnline

Brief title
Organ motion and early tumor response measurement

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
esophageal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: research afdeling radiotherapie

Intervention

Keyword: chemoradiotherapy, esophageal cancer, organ motion, tumor response

Outcome measures

Primary outcome

Primary endpoint of this study is to quantify motion of the esophageal tumor over the course of chemoradiation. Fiducial markers placed in the esophageal wall will be taken as surrogate position of the tumor. By matching the markers on the reference scan the motion variables can be obtained. These different variables are necessary to calculate the corresponding PTV margin. These motion variables are;

• Bony anatomy setup error, this is defined as the discordance between the patient*s position from baseline treatment planning position by external fiducial markers and the bony setup correction deriving from the CBCT

• Peak-to-peak amplitude of the GTV/CTV by breathing motion

• Baseline shifts (inter and intra fraction)

• Inter-fraction motion; defined as the motion in between 2 radiation fractions

• Intra-fraction motion; defined as the motion occurring within the time period of a single daily fraction

Secondary outcome

• Peak to peak amplitudes of mid-thoracic versus distal/ GE-junctional tumors

• Correlation of tumor response on FDG-PET scan (SUV decline) and DCE-MRI (change in Ktrans) with pathological response for trimodality patients

• Correlation of combined PET and DCE-MRI results with pathological response for trimodality patients

• SUVmax of the primary tumor on 3D versus 4D PET

• DCE*MRI of the esophagus for treatment planning and response monitoring

•* Ease of insertion, migration and visibility of different fiducial markers

Study description

Background summary

We believe that the existing gap in knowledge on how to quantify target organ motion of the esophageal tumor and to rationally define appropriate PTV margins will provide clinically meaningful information in the design of subsequent multi-institutional multimodality trials for esophageal cancer. The esophageal tumor is rarely visible on conebeam CT (CBCT), however a fiducial gold marker has good visibility on CBCT and movement of these markers can be used as the surrogate for the esophageal tumor motion.
For optimal personalized treatment a combination of patient specific geometric uncertainty and response prediction during treatment could lead to personalized adaptive treatment.

It is our working hypothesis that quantifying geometrical uncertainties of motion will be necessary to calculate appropriate PTV margins and that upper/mid thoracic esophageal tumors have smaller geometric uncertainties due to less respiratory motion compared to distal/GEJ tumors and therefore require a smaller PTV margin, and that motion-corrected multimodal response evaluation may better predict outcome.
Further we hypothesize that early imaging of the response at chemoradiotherapy by MRI, PET or combined results could identify patients who will (not) respond at this treatment and will (not) benefit from the planned treatment.

However, the distal border of a stenotic esophageal tumor cannot be reached by the relatively thick EUS, but the much thinner gastro scope often can. During insertion of the gold fiducial marker, the marker is pushed out of the stylet and slides true a couple of mm of tissue. As other organs are in close proximity of the esophagus, insertion of gold fiducials is only safe during EUS visualization.

Study objective

To quantify motion based variation of the target volume of the primary tumor over the course of chemoradiotherapy in esophageal cancer patient, and to use this information to calculate appropriate PTV (planning target volume) margins according to the margins recipe for patients receiving trimodality (neoadjuvant

chemoradiation and surgery) or definitive chemoradiation in order to personalize radiation treatment, resulting in either better target coverage or a reduction in normal tissue radiation exposure.

Study design

A single center prospective observational study will be performed in esophageal cancer patients. This study registers motion of the esophageal tumor, using 4D planning CT scans and repeated 4D CBCT scanning. Motion of fiducial markers inserted into the esophageal wall, will be used as a surrogate for tumor motion in the limited image quality of CBCT scans.
Patients planned for trimodality treatment will additionally be imaged by serial 4D PET CT and MRI in week 0 (before start chemoradiotherapy), week 3 (during chemoradiotherapy) and week 10 (just prior to surgery) to observe (early) signs of tumor response.
Patients planned for definitive chemoradiation will not receive extra MRI imaging during treatment because of the inability to correlate this imaging with pathological response.

Study burden and risks

Placement of the fiducial markers will be performed during a regular staging procedure (with informed consent). The duration of EUS will increase due to the marker placement. No adverse events are expected by marker placement other than the regular risks of EUS-FNA. EUS-FNA is considered a safe staging procedure with a morbidity of < 1%
The variability of the position of the esophageal tumor will be quantified by the standard 4D-CT scan during the radiotherapy treatment preparation phase and repeated 4D-CBCT scans during the course of treatment. Accordingly to standard procedures, CBCT scans will be made right before the first 3 fractions and thereafter weekly 4D-CBCT scans will be made. For the patients within this trial daily CBCT scanning will be performed.
Patients treated with trimodality will receive an extra FDG PET scan during treatment. This requires the patient to fast 6 hours before scanning and gives additional imaging dose. The total additional imaging dose associated with the additional CBCT images and the additional FDG PET scan equals about 1% of the treatment dose. This is similar to the calculation accuracy of state of the art treatment planning systems and is thus considered to be negligible.
The additional PET scan and MRI scans will be combined with other appointments in the hospital, but will take about 30 minutes per MRI scan and about 1,5 hours for the PET scan.

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

• Histologic evidence of invasive adenocarcinoma or squamous cell cancer of the esophagus
• Patient eligible for trimodality treatment (chemoradiotherapy and surgery) or definitive chemoradiotherapy
• T3N0M0 or T1-4N1-3M0. Patients with M1 disease solely on the basis of supraclavicular metastasis and not a junction tumor as primary are eligible. (AJCC 7th edition)
• WHO performance status <= 2
• Clinically operable for R0 resection in the opinion of an experienced upper gastrointestinal or thoracic surgeon for patients planned for trimodality
• Tumor localization at least 2cm from the upper esophageal sphincter and invading no more than 5cm into gastric cardia
• • Age >= 18 years
• Written informed consent before endoscopy or EUS

Exclusion criteria

• Prior treatment with thoracic surgery or thoracic radiotherapy
• Pregnancy
• Severe cardiopulmonary restriction

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):	18-04-2014
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	03-12-2013
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	22-07-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-02-2017
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	29-06-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2018
Application type:	Amendment
Review commission:	METC NedMec

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	NL45839.031.13