TOwards Personalized multi-modality esophageal cancer treatment using machine learning-based Quantitative MRI

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Primary:Sub-study I:- To develop high-quality fast quantitative MRI protocol for multi-contrast imaging of tumour pathophysiology at 3T in esophageal cancer patientsSub-study II:- To determine inter- & intra-session test-retest characteristics...

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

Summary

ID

NL-OMON56160

Source
ToetsingOnline

Brief title
TOP-QMRI

Condition

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

Synonym
esophageal cancer, tumour pathophysiology

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: KWF

Intervention

Keyword: esophageal cancer, machine learning, personalized medicine, quantitative MRI

Outcome measures

Primary outcome

Sub-study I:No quantitative endpoints will be derived. Success will be defined as having a high-quality fast quantitative MRI protocol for multi-contrast imaging of tumour pathophysiology at 3T. This includes: visibility of tumor tissue on the individual MR images, visibility of tumor tissue on the derived quantitative MRI parameter maps and adequate signal to noise ratio in the tumor tissue

Sub-study II: Inter- & intra-session repeatability coefficient are assessed, based on the standard deviation of repeated measures, indicating 95% CI of repeated measures.

Sub-study III: The effect size of quantitative MRI parameters: f at MRI-1, Ktrans at MRI-1, ΔD from MRI-1 to MRI-3 for prediction of the presence of residual tumor in the ex vivo surgical specimen in individual esophageal cancer patients

Secondary outcome

Sub-study II:

- Inter- & intra-session coefficient of variation for the repeatability are assessed, indicating variation of the measurement compared to the mean in percentages.

- Baseline characteristics (mean and standard deviation) on the quantitative MRI parameter maps (D, D*, f, T2*, T2 and T1) of the esophageal tumor.

Sub-study III:

- Area under the curve (AUC) of receiver-operator characteristic (ROC) analysis of quantitative MRI parameters at MRI-1, MRI-2, MRI-3 for prediction of the presence of residual tumor in the ex vivo surgical specimen in individual esophageal cancer patients.

- Spatial correlation of quantitative MRI parameters to histopathology of ex vivo surgical specimens

- Response of quantitative MRI parameters (D, D*, f, Ktrans, Kep, Ve, Vp, T2*, T2 and T1) to neoadjuvant therapy on individual esophageal cancer patients

- Correlation between the baseline quantitative MRI parameters (D, D*, f, Ktrans, Kep, Ve, Vp, T2*, T2 and T1) and treatment efficacy (MRI1)

- Correlation between the change in quantitative MRI parameters (D, D*, f, Ktrans, Kep, Ve, Vp, T2*, T2 and T1) and treatment efficacy (MRI1, MRI2 & MRI3)

- Correlation between the quantitative MRI parameters (D, D*, f, Ktrans, Kep, Ve, Vp, T2*, T2 and T1) and 18-F-FDG-PET-CT parameters

Study description

Background summary

Esophageal carcinoma is amongst the world*s most prevalent and fatal malignancies, with an overall 5-year survival rate of less than 20%. Since the CROSS trial, most patients with resectable esophageal cancer are treated with chemotherapy and radiotherapy, so-called, neoadjuvant chemoradiotherapy (nCRT), followed by surgery. However, the median overall survival after nCRT + surgery is only four years. Furthermore, long-lasting (10+ years) deterioration in the quality of life has been described after curative esophageal cancer surgery. Conversely, 29% of patients who underwent esophageal cancer surgery had a pathological complete response (pCR) after nCRT. These complete responders risk serious complications from extensive surgery that they do not require.

Therefore, other treatments, such as definitive CRT, are investigated. Treatments could become substantially more efficient if we can personalize treatment and identify which patients benefit from a more intensive treatment regime (to improve survival) and which patients could safely be treated with a less intensive treatment regime (to improve quality of life). Current imaging techniques (CT, PET-CT, EUS) have substantial limitations for predicting response. Thus, novel biomarkers are urgently needed to guide and personalize treatment. Quantitative magnetic resonance imaging (MRI) is a versatile technique that measures tumour pathophysiology non-invasively. MRI can play a major role in patients with esophageal cancer, particularly for treatment response prediction and monitoring. Several studies at expert centres, including the Dutch PRIDE study, are investigating the use of quantitative MRI for response assessment after nCRT. These studies show promising results for DWI, DCE and T2* MRI for identifying responding patients at an early treatment stage. Most studies highlighted the need for improving quantitative imaging techniques and adding motion management. Reasons for poor image quality are the presence of cardiac and respiratory motion. Furthermore, the esophagus and the esophageal have a small diameter, necessitating high-resolution imaging. We hypothesize that improved quantitative MRI technologies might be able to accurately visualize tumour pathophysiology in esophageal cancer and thereby aid to substantially improve patient tailored treatment of esophageal cancer.

Study objective

Primary:
Sub-study I:
- To develop high-quality fast quantitative MRI protocol for multi-contrast imaging of tumour pathophysiology at 3T in esophageal cancer patients

Sub-study II:
- To determine inter- & intra-session test-retest characteristics of optimized quantitative MRI in esophageal cancer patients

Sub-study III:
- validate optimized quantitative MRI for prediction of the presence of residual tumor in the ex vivo surgical specimen in individual esophageal cancer patients

Secondary:
Sub-study II
- Determine typical baseline characteristics of quantitative MRI parameters in esophageal cancer patients
Sub-study III
- Perform spatial correlation of quantitative MRI parameters to histopathology of ex vivo surgical specimens

- Characterize the response of quantitative MRI parameters to neoadjuvant therapy on individual esophageal cancer patients
- To investigate whether there is a relation between the baseline quantitative MRI parameters and treatment efficacy (MRI1)
- To investigate whether there is a relation between the change in quantitative MRI parameters and treatment efficacy (MRI1, MRI2 & MRI3)
- To investigate the relation between the quantitative MRI parameters and 18-F-FDG-PET-CT parameters

Study design

Prospective single-center cohort study

Study burden and risks

Participation in this study does not lead to an immediate advantage for the participant. The
overall aim of the TOP-QMRI project is to develop a quantitative MRI technique that could provide further insight into treatment efficacy for esophageal cancer patients.

The risks of this study are expected to be low and contains the risk associated with the infusion of Dotarem (Gadoteric acid) contrast injection (hypersensitivity reactions or hypotension). The decision to participate in the study or not will not delay or otherwise influence the treatment trajectory for patients. Where possible, we will aim to plan scans on days that the patients are already visiting the Amsterdam UMC for regular treatment.

Sub-study I: 1 MRI. Time invested by the patient for participating in this study will approximate (MRI-scan time 75 minutes) 1 hour and 15 minutes.
Sub-study II: 2 MRI at 2 different moments in time. Both MRIs will take place before neoadjuvant treatment. Time invested by the patient for participating in this study will approximate (MRI-scan time 75 minutes) 2 hours and 30 minutes.
Sub-study III: 3 MRIs at 3 different moments in time. The first MRI will take place before neoadjuvant treatment, the second MRI two weeks after the start of neoadjuvant treatment and the third MRI before esophagectomy. Time invested by the patient for participating in this study will approximate (MRI-scan time 75 minutes) 3 hours and 45 minutes.

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

1. Patients with biopsy-proven esophageal cancer (adenocarcinoma)
2. WHO-performance score 0-2.
3. Written informed consent.

For sub-study III, subjects must also meet the following criterium:
4. Planned for neoadjuvant therapy and surgery with curative intent (cT1-4a, N0-3, M0)

Exclusion criteria

1. Contra-indications for MR scanning.
2. Age < 18 years

Potential subjects who meet the following criterium will be excluded from participation in this study:
3. Contra-indications for Gadolinium-based contrast injection, including known renal insufficiency (eGFR<30 ml/min/1.73m2) and known allergic reaction to

gadolinium-based contrast agent.

For sub-study III, potential subjects who meet the following criterium will be excluded from participation in this study:
4. Previous treatment for esophageal cancer

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):	22-01-2024
Enrollment:	65
Type:	Actual

Medical products/devices used

Generic name:	MRI sequences
Registration:	No

Ethics review

Approved WMO Date:	25-10-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-01-2025
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	NL83772.018.23