# Innovative MRI techniques to improve treatment stratification of patients with Esophageal cancer: an optimization and pilot study

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1. To determine the optimal acquisition technique for USPIO enhanced MRI (without contrast injection), DCE (without contrast injection) and DWI and T2* MRI of esophageal cancer in terms of signal-to-noise ratio, time resolution and spatial…

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Gastrointestinal neoplasms malignant and unspecified |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON44292

**Source**
ToetsingOnline

**Brief title**
IMPROVE

### Condition

- Gastrointestinal neoplasms malignant and unspecified

**Synonym**
Esophageal cancer, esophageal tumor

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** Maag Lever Darm stichting

## Intervention

**Keyword:** Esophageal caner, Lymph nodes, MRI, USPIO

## Outcome measures

### Primary outcome

For USPIO MRI the main endpoint is the change in T2 and T2* at the tumor and

lymph nodes on MRI after the administration of USPIO.

For DWI the main endpoint is the perfusion fraction f and the diffusion

coefficient D obtained by IVIM of the primary tumor.

For T2* MRI the main endpoint is T2* of the primary tumor.

For DCE MRI the main endpoint is the 'transfer constant' Ktrans and 'rate

constant' kep, of the (remaining) primairy tumor

### Secondary outcome

Correlation of the MRI findings with pathology

# Study description

### Background summary

The outcome of esophageal cancer is poor, with an overall 5-year survival rate of 10% worldwide. In resectable esophageal cancer, outcome can be improved by multimodality treatment. The current standard treatment of resectable esophageal cancer consists of neoadjuvant chemoradiation followed by resection. In the Netherlands, the preferred chemoradiation regimen consists of carboplatin plus paclitaxel with concurrent radiotherapy in 23 fractions of 1.8 Gray.1 In a meta-analysis the benefit of chemoradiation over surgery alone for both adenocarcinoma and squamous cell carcinoma has been shown.2 However, not all patients benefit from this preoperative treatment regimen. Some patients develop recurrent disease despite chemoradiation and additional (systemic) treatment might have been indicated. In contrast, in other patients a (nearly) complete response is observed after chemoradiation and those patients could

possibly have been treated with a less extensive treatment regimen. Furthermore, in patients without a threatened circumferential resection margin (CRM) and lymph node metastases chemoradiotherapy could possibly be omitted, reducing patients* risk for complications and unnecessary, expensive treatment. Thus, stratification of patients with esophageal cancer is urgently needed. Functional magnetic resonance imaging techniques (MRI) can provide in vivo, quantitative information on tumor biology and may prove to be a useful non-invasive tool for this purpose. In this project, ultra-small superparamagnetic particles of iron oxide (USPIO) enhanced MRI using iron-dextran nano particles, diffusion weighted MRI (DWI) and T2* MRI will be developed, both in terms of improvement of acquisition and data processing techniques. For patients with esophageal cancer, the proposed acquisition techniques and data processing have not been performed before.

## Study objective

1. To determine the optimal acquisition technique for USPIO enhanced MRI (without contrast injection), DCE (without contrast injection) and DWI and T2* MRI of esophageal cancer in terms of signal-to-noise ratio, time resolution and spatial resolution.
2. To determine the optimal data processing approach for USPIO enhanced MRI, DCE, DWI and T2* MRI of esophageal cancer.
3. To explore the correlation between lymph node involvement on USPIO enhanced MRI in relation to results obtained at pathological examination.
4. To explore the correlation of DCE, DWI and T2* MRI of esophageal cancer in relation to stromal involvement and markers of hypoxia and vasculature obtained at pathological examination.
5. To explore the accuracy of MRI concerning circumferential tumor delineation compared to pathological examination.
6. To determine the feasibility to detect lymph node involvement on USPIO enhanced MRI in initial staging, prior to preoperative chemoradiation therapy.
7. To determine the correlation between lymph node involvement on pre-treatment USPIO MRI in relation to results obtained at pathology after complete treatment.

## Study design

The project will be executed in three steps:
1) Optimization of acquisition and data processing techniques of USPIO MRI (without contrast injection), DCE (without contrast injection), DWI and T2* in five healthy volunteers to optimize field of view, number of slices, slice thickness (objectives 1 and 2).
2) Using the data of (1): assessment of USPIO MRI, DCE, DWI and T2* MRI in 20 esophageal cancer patients with clinically suspect lymph nodes directly before surgery (objectives 3, 4 and 5).
3) Using the data of (1): assessment of USPIO MRI, DCE, DWI and T2* MRI in 10

esophageal cancer patients with clinically suspect lymph nodes, before initial start of the treatment (objectives 6 and 7).

**Study burden and risks**

Patients will have no direct benefit from the study.

The administration of Gadolinium involves a very small risk of an acute allergic reaction.

The most important side effects of intravenous iron injection are hypotension and severe hypersensitivity reactions. These side effects are rare. We try to further decrease the risk by excluding patients and healthy volunteers that had hypersensitivity reactions before. Because hypersensitivity reactions will only occur shortly after administration, we monitor each patients and healthy volunteer for at least 30minutes after injection. Furthermore, medication to treat hypersensitivity reactions will be available during the examination. Other, less severe side-effects of iron administration include nausea, diarrhea, constipation, dizziness and thickening of the legs.

The administration of Buscopan involves a risk of an adverse reaction. The most common adverse reactions are accommodation disorders, tachycardia, vertigo and a dry mouth. Patients who have a contraindication for IV administration of Buscopan (mega-colon, ileus, myasthenia gravis, glaucoma, prostate hypertrophy with urine retention, intestinal stenosis and tachycardia), will undergo the scans without administration of Buscopan.

For injection of the USPIO a temporary IV canule will be injected once.
A group of 30 patients will visit the AMC twice for study purposes. Where possible these visits will be combined with the visits planned for standard patient care.
One group of 5 healthy volunteers will visit the AMC once for a MRI scan.
One group of 5 patients will visit the AMC once for a MRI scan.

# Contacts

**Public**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
**Scientific**
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Volunteers:
• Written informed consent.;Patients:
• Patients with biopsy proven esophageal cancer (squamous cell carcinoma or adenocarcinoma).
• Suspected nodal involvement on EUS or CT at diagnosis.
• WHO-performance score 0-2.
• Scheduled for surgery.
• Written informed consent.

## Exclusion criteria

• Any psychological, familial, sociological or geographical condition potentially hampering adequate informed consent or compliance with the study protocol.
• Contra-indications for MR scanning, including patients with a pacemaker, cochlear implant or neurostimulator; patients with non-MR compatible metallic implants in their eye, spine, thorax or abdomen; or a non-MR compatible aneurysm clip in their brain; patients with severe claustrophobia.
• Active inflammatory diseases
• History of anaphylaxis or other hypersensitivity reactions
• History of iron overload
• History of abnormal liver function, or elevated liver enzymes (ALAT, ASAT > 3 times upper limit of normal)
• Elevated Serum Transferrin Saturation (TSAT) (>50%) or hemoglobin (>10.5mmol/L)

• Deminished kidney function (eGFR<60)

# 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): | 28-04-2015 |
| Enrollment: | 40 |
| Type: | Actual |

# Ethics review

Approved WMO

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|---|---|
| Date: | 20-06-2014 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |

Approved WMO

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|---|---|
| Date: | 26-02-2016 |
| 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 | NL48757.018.14 |