In vivo assessment of hypoxia in gastro-intestinal cancer using 18F-HX4-PET: an optimization and reproducibility study

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In this study, we first intend to investigate the optimal time point for measurement of hypoxia in esophageal, pancreatic and rectal cancer using 18F-HX4-PET and then assess reproducibility of hypoxia measurements in these tumor types.

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

Summary

ID

NL-OMON37773

Source
ToetsingOnline

Brief title
Reproducibility of hypoxia measurment in GI cancer.

Condition

- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cancer, HX4, hypoxia, PET

Outcome measures

Primary outcome

The primary endpoints are the optimal time point for 18F-HX4-PET scanning and the reproducibility of hypoxia measured non-invasively in vivo with 18F-HX4-PET.

Secondary outcome

Secondary endpoints are correlations of levels of hypoxia measured by 18F-HX4-PET with endogenous hypoxia markers determined by immunohistochemistry (HIF1-alfa, CA9, PAI-1, VEGF) in pretreatment tumor biopsies or surgical specimens and with pathological response to treatment in surgical specimens after neo-adjuvant treatment.

Study description

Background summary

Several studies have shown that tumour hypoxia may have a negative impact on the outcome of anticancer treatment. Assessment of tumor hypoxia at baseline or shortly after start of treatment may serve as a predictive marker to determine treatment efficacy at an early stage. Preferably, such an assessment is performed in vivo and non-invasively.Non-invasive imaging with positron emission tomography (PET) using the 2-nitroimidazole nucleoside analogue, 3-18F-fluoro-2-(4-((2-nitro-1H-imidazol-1-yl)methyl)-1H-1,2,3-triazol-1-yl)propan-1-ol (18F-HX4), was tested as a new marker of tumor hypoxia. Before hypoxia-measurements can be clinically implemented for response prediction, the reproducibility of the technique should be assessed for each specific tumor type. Knowledge of reproducibility is needed to determine what change in parameters between two examinations can be considered relevant in an individual patient. Assessment of reproducibility becomes even more important in early response monitoring since the changes in the tumor induced by the treatment may

be smaller during the treatment compared to response monitoring after completion of treatment. Also, as image quality of 18F-HX4-PET increases with increasing time intervals after injection, determination of the optimal time point for measurement of hypoxia is warranted.

Study objective

In this study, we first intend to investigate the optimal time point for measurement of hypoxia in esophageal, pancreatic and rectal cancer using 18F-HX4-PET and then assess reproducibility of hypoxia measurements in these tumor types.

Study design

In this study two steps will be taken.
1) First, as 18F-HX4-PET image quality may improve when allowing for relatively longer time intervals after injection, in three patients with esophageal, pancreatic or rectal cancer 18F-HX4-PET scans will be performed 90, 180 and 240 minutes after injection of 18F-HX4. The time-point with the best image quality (in terms of tumor-to-background-ratio) will be chosen for the reproducibility study.
2) In the second step, patients with proven esophageal, pancreatic or rectal cancer will undergo an 18F-HX4-PET twice within one week before start of treatment. 18F-HX4-PET will be performed at 90, 180 or 240 minutes after injection of 18F-HX4, depending on the results of the first part of the study. Reproducibility of hypoxia measured by 18F-HX4-PET will be assessed. In those patients for whom tumor tissue is available which has not been treated with radiation or chemotherapy, levels of hypoxia measured by 18F-HX4-PET will be compared with endogenous hypoxia markers (HIF1-alfa, CA9, GLUT1, PAI-1, VEGF) using immunohistochemistry. In those patients that underwent 18F-HX4-PET before start of neoadjuvant treatment, levels of hypoxia measured by 18F-HX4-PET will be compared to pathological response after neoadjuvant treatment.

Study burden and risks

The patient will not have a direct benefit from the study The proposed 18F-HX4 dose is chosen based on the phase 1 study with 18F-HX4.22 In this phase I study no toxicities were observed except for a mild, grade I headache one day after 18F-HX4 injection, which was considered unlikely to be related to the injection. In view of previous experiences with 18F-HX4, conventional PET-CT and other nitroimidazole drugs, we expect no unforeseen side effects. Nevertheless, it cannot be excluded that patients will experience an acute allergic reaction to 18F-HX4. Therefore, all patients will be monitored carefully during and directly after administration of the labelled 18F-HX4 by trained caregivers.
Participation in the study will involve radiation exposure which is

estimated to be maximally 12,4 mSV for the two scans together. The theoretical chance for radiation induced cancer induction is 5% per Sievert. For a radiation exposure of 10 mSv this implies a chance of 1 in 2000. This number applies to patients of 30 years old. The risk reduces with ~50% for a typical oncological population of patients aged 55-70 years. Moreover, all patients with rectal cancer and esophageal cancer in this protocol will be treated with radiotherapy according to the current clinical guidelines. Radiation exposure due to the 18F-HX4 scans is negligible compared to radiation exposure because of the clinically indicated radiotherapy.
Finally, patients will have to come to the hospital twice for a 18F-HX4-PET scan. One hour after injection of 18F-HX4 patients will be scanned for approximately 15 minutes. The total extra time spent in the hospital will be ~4 hours at most on two separate days.

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

- Patients with biopsy proven invasive carcinoma of the esophagus, pancreas or rectum. In pancreatic cancer cytological proof or a high suspicion on CT imaging is allowed, too.
- Any tumor with a size * 1cm
- WHO-performance score 0-2
- Written informed consent

Exclusion criteria

- Any psychological, familial, sociological or geographical condition potentially hampering adequate informed consent or compliance with the study protocol.
- Surgery, radiation and/or chemotherapy foreseen within the timeframe needed for two PET scans.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2012
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	25-05-2012
Application type:	First submission

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	NL40274.018.12