Non-Ionizing Metabolic Imaging using robust phosphorus MRI to predict treatment efficacy.

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Primary objectives pancreatic cancer:• In this clinical pilot study, we will assess the effect size to perform a power calculation for a subsequent clinical trial. Therefore we want to evaluate the ability of metabolic 7T MRI imaging to determine...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neoplastic and ectopic endocrinopathies
Study type	Observational invasive

Summary

ID

NL-OMON55194

Source
ToetsingOnline

Brief title
NIMI study

Condition

- Neoplastic and ectopic endocrinopathies
- Endocrine neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
Pancreatic cancer and lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: Applied and Engineering Sciences,KWF

Intervention

Keyword: 7 Tesla MRI, Metabolic imaging, Pancreatic/lung cancer, Spectroscopy

Outcome measures

Primary outcome

The main study parameter is the change in metabolic ratio of the phospholipid metabolites PC, PE, PGE, GPC, Pi, PCr, and energy metabolites ATP from the area under the curve (AUC) of the corresponding spectral peaks between the measurements at baseline (healthy volunteers), before-, during- (patients with pancreatic cancer) and after treatment (chemotherapy or immunotherapy). From patients who underwent surgery (only pancreatic cancer patients), tumor characteristics (pathology results using CAP scoring system32, location of tumor, stage at time of diagnosis) will be assessed to correlate with metabolite ratios in order to make a distinction between tumor biology (based on pathology result; aggressive or non-aggressive tumor) and their response to chemotherapy.

Secondary outcome

The secondary study parameters and endpoints will be 6 and 12 month disease control rate (DCR) according to internationally accepted response evaluation guidelines (RECIST 1.1) and potential surgery outcome (pancreatic cancer patients) based on CT-imaging (division based on the DPCG-criteria30). For the lung cancer cohort, pulmonary toxicity will be scored (secondary objective). Phosphorus MRSI will be used to estimate an effect size for potentially predicting (non)-response and occurrence of severe side-effects of therapy.

Multi-variable analysis of clinically relevant data to investigate the feasibility of a dynamic prediction model will use all metabolic imaging data, size measurements from CT, conventional 7T MR imaging scans, coded radiology reports, clinical patient data, details extracted from clinical notes which are coded before storage to preserve anonymity, choice of therapy, progression free survival (PFS) and overall survival (OS).

Study description

Background summary

Cell proliferation and energy metabolism are the main hallmarks of tumor biology. State of the art imaging techniques can indirectly obtain insight in cell proliferation using diffusion weighted MRI, while FDG-PET can obtain information of glucose uptake hence reflecting energy demand. Here we will investigate the use of 31P MRSI as a non-ionizing and more direct imaging technique to detect cell proliferation and energy metabolism at once, aiming for a better, faster, non-invasive and less expensive readout of treatment effects.
Proof of principle studies in breast cancer in our center have demonstrated that the accuracy of 31P MRSI in predicting non-responders to chemotherapy improved from 75% to 96% when compared to biopsy histopathology and traditional imaging. To make this technology widespread available and economically viable, use of 31P MRSI should extend beyond exclusively breast cancer and also potentially guide treatment for prostate, colon, rectum, pancreas, liver and lung tumors.
In contrast to 31P breast MRSI, 31P MRSI of deeper laying (moving) organs requires an array of 31P receivers, needs to be robust for motion artefacts, and manage field non-uniformities. Leveraging on earlier investments in hardware, we will design and investigate the use of snapshot 31P MRSI guided by motion and field navigators to detect cell proliferation and energy metabolism in tumors during treatments. Moreover, as 31P signals are basically unaffected by traditional 1H MRI, novel scan merging technologies of Philips will be implemented to obtain the 31P MRSI simultaneous with anatomical 1H MRI, resulting in short scan sessions. In our study, we will target the most challenging organs for MRI (i.e. pancreas and lung) to determine robustness of 31P MRSI and assess the effect size of predicting treatment efficacy in a pilot study with patients scheduled for treatment of pancreas and lung cancer.

Study objective

Primary objectives pancreatic cancer:
• In this clinical pilot study, we will assess the effect size to perform a power calculation for a subsequent clinical trial. Therefore we want to evaluate the ability of metabolic 7T MRI imaging to determine tumor response on FOLFIRINOX chemotherapy in pancreatic cancer

Secondary objectives pancreatic cancer:
• To compare diagnostic accuracy of 7T MRI to conventional CT-imaging in pancreatic cancer
• To predict surgical resectability of pancreatic cancer with metabolic 7T MRI
• To investigate the correlation of tumor characteristics (pathology result, location of tumor, stage at diagnosis etc.) with measured levels of 31P metabolites that are involved in energy metabolism and cell proliferation (e.g. ATP, inorganic phosphate phosphocholine, phosphoethanolamine, glycerolphosphocholine, glycerophosphoethanolamine) gained from the metabolic 7T MRI

Primary objective lung cancer:
• In this clinical pilot study, we will assess the effect size to perform a power calculation for a subsequent clinical trial. Therefore, we want to determine whether metabolic imaging at 7 Tesla is feasible and suitable to detect changes in phospholipid metabolism and ATP levels in patients with advanced non-small cell lung cancer after treatment with immune checkpoint inhibitors to predict treatment outcome.

Secondary objectives lung cancer:
• In this study we will perform a baseline 31P MRI
• Determine the metabolic change caused by the systemic therapy with checkpoint inhibitors in relation to the variance of metabolite levels between patients prior to treatment.

• Relate metabolic signature to clinical outcome and occurrence of side-effects

Study design

In this single-centre observational cohort study, patients with (borderline) resectable- or locally advanced pancreatic cancer treated with FOLFIRINOX yet selected for surgery and patients with lung cancer treated with immunotherapy will be asked for participation in the study. Additionally, 15 healthy volunteers will be scanned once to perform a baseline for the metabolic ratio of phospholipid metabolites (control group pancreatic cancer). After eligible patients have signed informed consent, patients will continue to receive standard treatment as scheduled. For patients with pancreatic cancer, a standard CT-scan will be made after four courses of FOLFIRINOX, and will be

supplemented with NIMI-scans on the same day. The scans will be made before-, after one cycle with FOLFIRINOX and after four cycles with FOLFIRINOX (Figure 1). Phosphorus MRSI combined with anatomical MRI will be obtained in the same scan session.
Patients with lung cancer will be scanned twice, once just before immunotherapy, and once 3 to 6 weeks after the start of the therapy (Figure 2). The duration of the study depends on the inclusion of the required number of subjects, with an expected overall duration of 24 months.

Study burden and risks

Patients will be asked for two or three hospital visits to undergo imaging during approximately one hour. A healthy volunteer will be asked for one hospital visit to undergo one MRI scan. To avoid an *extra* visit to the hospital, we will try to plan the MRI scans on days that a patient already has an appointment in the hospital. The patient will not have a direct benefit of the study. Recently, many studies have investigated the safety of ultra-high field MRI, such as 7 Tesla MRI, including potential side-effects35. Moreover, in other countries these ultra-high field MRI*s have been used since the 90s. Up until now, no negative effects have been found and the only reported complaints are temporary vertigo and nausea during scanning. These side-effects can be attributed to the fact that the vestibular system confuses the changing magnetic field with movement.

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

Inclusion criteria for pancreatic cancer:
To be eligible to participate in this study, a subject must meet all of the following criteria:
• Patients with (borderline) resectable- or locally advanced pancreatic cancer, with histological or cytological proof, scheduled for standard of care chemotherapy containing fluorouracil, oxaliplatin, irinotecan and leucovorin (FOLFIRINOX) as assessed by a medical oncologist.
• Tumour size >= 1cm.
• WHO-performance score 0-1, weight >=40kg
• Written informed consent.

Inclusion criteria healthy volunteers (control group pancreas cohort):
In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Healthy volunteers; No history of cancer, no history of chronic diseases, no history of a pancreatic disease, no elective surgery <8 weeks
• Age: >= 18yrs
• WHO-performance score 0-2.
• Written informed consent.

Inclusion criteria for lung cancer:
In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• Patients with non-small cell lung cancer, with histological or cytological proof, scheduled for immune checkpoint inhibitors
• Tumour size >= 2cm.
• WHO-performance score 0-2, weight >=40kg
• Written informed consent.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Any psychological, familial, sociological, or geographical condition potentially hampering adequate informed consent or compliance with the study protocol.
• Contra-indications for 7T 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 claustrophobia and/or obesitas.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-02-2022
Enrollment:	45
Type:	Actual

Medical products/devices used

Generic name:	7T MRI
Registration:	No

Ethics review

Approved WMO Date:	22-01-2021
Application type:	First submission
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	NL74729.041.20