Non-invasive MRI spectroscopy at 7 Tesla in lymphoma

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lymphomas NEC
Study type	Observational invasive

Summary

ID

NL-OMON40364

Source
ToetsingOnline

Brief title
MRI spectroscopy in lymphoma

Condition

- Lymphomas NEC
- Lymphomas NEC

Synonym
lymphoma; lymph node cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Lactate, Malignant lymphoma, MRI spectroscopy, Phospholipids

Outcome measures

Primary outcome

The primary endpoint is the diagnostic accuracy of the 7T MRI spectroscopy biomarkers lactate and phospholipids for the differentiation between aggressive and indolent lymphoma. In addition, levels of lactate and phospholipids will be correlated with Ki-67 expression and the maximum standard uptake value (SUVmax) of 18F-FDG PET.

The secondary endpoint of this study is to determine interscan agreement (i.e. test-retest variability) of 7T MRI spectroscopy for assessing levels of lactate and phospholipids in lymphoma.

The tertiary endpoint is to determine the difference in lactate and phospholipid concentrations between two different lymph nodes.

The fourth endpoint is the determination of presence and degree of changes in levels of lactate and phospholipids after treatment relative to pretreatment values.

Secondary outcome

not applicable

Study description

Background summary

Metabolites like lactate and phospholipds are associated with tumor aggressiveness, response to therapy and prognosis of several cancers. With 7 Tesla 1H and 31P magnetic resonance imaging (MRI) spectroscopy these metabolites can be detected non-invasively. The lymphomas comprise a heterogeneous group of tumors with a very variable biology and prognosis, ranging from very indolent to highly aggressive. If MRI spectroscopy can differentiate between aggressive and indolent lymphoma non-invasively, this could have an important impact on patient management. For instance, MRI spectroscopy findings suggestive for aggressive lymphoma in a patient with biopsy- proven indolent lymphoma, will indicate either a redirected biopsy or a more intensive treatment. This would also support the development of a full-body MRI spectroscopy set-up at 7T to realize multiple "metabolic biopsies" in different organs in one scan session. Advantages of this method compared to biopsy and pathological examination are its non-invasiveness, its repeatability (making it suitable for follow-up examinations) and the provision of spatial information via MRI spectroscopic imaging (thereby taking into account tumor hetereogeneity amongst lymph nodes). The second objective of this study is to assess interscan agreement (i.e. test-retest variability) of 7T spectroscopy for the quantification of lactate and fosfolipids. Therefore, in the first 30 patients, the scan performed before treatment will be repeated to assess the degree of correlation with the previous assessment of the same lymph node. Tumor heterogeneity amongst lymph nodes in lymphomas is not uncommon. In the present study difference in concentration of lactate and phospholipids between lymph nodes will be assessed. Therefore the last 30 patients will be scanned twice before therapy and concentrations of lactate and phospholipids in two different lymph nodes will be assessed. The final object of the present study is to assess changes in lactate and phospholipid concentrations shortly after the start of treatment compared to pretreatment values to analyse the feasibility of this technique for early therapy response assessment in patients with various pathological subtypes of lymphoma. Previous animal experiments showed that the concentration of lactate and phospholipids changed significantly after start of treatment. This suggests MRI spectroscopy can be used as a tool for early response assessment. Patients who are unlikely to respond to therapy can consequently be directed to another therapy. In order to determine the feasibility of MRI spectroscopy for early response assessment, patients with various pathological subtypes of lymphoma will be scanned before and shortly after start of therapy. In all patients, changes in concentration of lactate and phospholipids relative to pretreatment values will be determined to analyse feasibility of MRS for the assessment of early therapy response in various pathological subtypes of lymphoma. A positive outcome of this feasibility study will justify the execution of future large-scale studies in

specific lymphoma subtypes that are treated with more homogeneous therapies.

Study objective

The primary objective of this project is to investigate whether 7T MRI spectroscopy biomarkers lactate and phospholipids can differentiate between aggressive and indolent lymphoma non-invasively.
The secondary objective of this study is to assess interscan agreement (i.e. test-retest variability) of 7T MRI spectroscopy for the quantification of lactate an phospholipids.
The tertiary objective is to assess degree of dissimilarity in lactate and phospholipid concentrations between two different lymphomatous lymph nodes in the same patient.
The fourth objective is to assess changes in levels of lactate and phospholipids shortly after the start of treatment in order to establish the feasibility of this technique for early therapy response assessment. A positive outcome of this feasibility study will justify the execution of future large-scale studies.

Study design

Patients eligible for enrolment in this, prospective, diagnostic cohort study are adults aged >= 18 years under high suspicion of or with histologically proven, newly diagnosed or relapsed Hodgkin or non-Hodgkin lymphoma with an enlarged (i.e. 2 >= diameter) lymphomatous lymph node in a superficial region (e.g. head/neck, axial or inguinal in order to fit in the MRI spectroscopy field of view). The hematologist will identify eligible participants, will inform them about the ongoing research and ask for their participation. All patients will undergo 1H and 31P MRI spectroscopy at 7T twice before and once within the first week after the start of treatment by using the 7T MRI located in the UMC Utrecht. In the first 30 patients MRI spectroscopy of the same lymph node will be performed twice before therapy to assess the interscan agreement. In the last 30 patients, MRI spectroscopy before therapy will be performed twice to assess lactate and phospholipids concentrations in two different lymph nodes to analyse tumor heterogeneity. 18F-FDG PET will be performed as part of standard clinical care. The tissue specimen that was acquired by excision/biopsy for diagnosis as part of standard clinical care will be additionally stained for Ki-67 in order to determine the proportion of dividing cells within the tumor. In order to determine the presence of early therapy-induced changes in the levels of lactate and phospholipids all patients will also undergo a 7T MRI spectroscopy scan within the first week after the start of treatment. Five-year follow-up data will be acquired of all patients in order to explore any potential correlation between levels of lactate and phospholipids and the progression free survival/overall survival.

Study burden and risks

The risk associated with the (radiation-free) MRI spectroscopy examinations is negligible and the burden can be considered minimal (no contrast agents will be applied and the patient just has to lie still in the scanner for approximately 40 minutes for each scan). To reduce the amount of anxiety and discomfort caused by scanning as much as possible, patients will be informed about the procedure.

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

- Male or female patients.
- Age: 18 years and older.
- Under high suspicion of or histologically proven, newly diagnosed or relapsed Hodgkin lymphoma or non-Hodgkin lymphoma.

- Patients are required to have an enlarged (i.e. diameter >= 2 cm) lymphomatous lymph node in a superficial region (e.g. head/neck, axial or inguinal in order to fit in the MRI spectroscopy field of view).
- Patients must be capable of giving written informed consent and the consent must have been obtained before the study-related procedures.

Exclusion criteria

- General contraindications to MRI (claustrophobia, cardiac pacemakers, neurostimulators).
- Patients with central nervous system lymphoma.
- Previous malignancy. However, subjects who have been free of malignancy for at least 5 years, or have a history of completely resected non-melanoma skin cancer, or successfully treated in situ carcinoma are eligible.
- Pregnant or lactating patients.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-11-2013
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	12-08-2013
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-04-2014
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL45669.041.13