Towards implementation of on-line MRI-guided radiation therapy in breast cancer patients

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To develop and evaluate an adaptive MRI-only workflow for the MR-linac treatment in breast cancer patients eligible for APBI, regional lymph node irradiation or a radiotherapy boost on tumor positive lymph nodes. Furthermore, to investigate whether...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON47005

Source
ToetsingOnline

Brief title
TIMBRE

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders

Synonym
breast cancer, breast malignancy

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: Breast cancer, MRI, MR-linear accelerator, Radiotherapy

Outcome measures

Primary outcome

1) Develop optimal MRI-sequences and an on-line adaptive MRI-only treatment planning workflow. 2) Investigate the feasibility of delineating tumor positive lymph nodes on MRI registered with the standard diagnostic FDG-PET scan and standard RT planning CT scan, compared to delineation based on standard RT planning CT scan and standard diagnostic FDG-PET scan.

Secondary outcome

Not applicable.

Study description

Background summary

In breast radiotherapy (RT), accelerated partial breast irradiation (APBI), instead of whole breast irradiation can represent less burdening alternatives in selected low-risk patients with equivalent therapeutic efficacy and reduced toxicity. Moreover, regional lymph node RT can replace axillary lymph node dissection (ALND) in patients with tumor positive (sentinel) lymph nodes. Current computed tomography (CT)-based image guided radiotherapy is not always optimal for these treatment approaches. Due to uncertainties in target volume definition on CT, relatively large RT treatment volumes are still required. Furthermore, delineation of individual lymph nodes before RT treatment, might be less accurate based on CT imaging. Magnetic resonance imaging (MRI) shows higher soft tissue contrast and visualizes breast glandular tissue and (tumor positive) lymph nodes better compared to CT. Hence, MRI techniques in RT supine position have been developed at the department of Radiation Oncology in UMC Utrecht, to visualize the tumor and axillary lymph nodes in breast cancer patients. The results of this study [METC-protocol 14-447] have been published recently. On MRI a significantly increased number of lymph nodes was visualized compared to CT. Therefore, MRI may increase the precision of delineation of individual (tumor positive lymph) nodes which could enable hypofractionated

dose escalation on the tumor positive lymph nodes instead of axillary surgery or conventionally fractionated RT. Furthermore, the results from this study showed that lymph node (LN) numbers on postoperative MRI were highly reproducible compared to the preoperative MRI. For that reason, both pre- and postoperative MRI scans could be used in the current study.
Recently, a hybrid system (MR-linac) consisting of a radiotherapy delivery device and an integrated MRI scanner (1.5 Tesla (T)), has been installed at the UMC Utrecht. The MR-linac has the potential to improve target definition and imaging during irradiation enabling a higher RT dose due to decreased margins and decreased RT target volumes. Therefore, the MR-linac may enable non-invasive RT and/or a shorter (i.e. hypofractionated) RT schedule as an alternative to current surgical treatment (e.g. in breast cancer patients eligible for APBI or in selected patients with an indication for regional lymph node irradiation). Consequently, treatment burden could be further minimized and quality of life could be increased in these patients.

Study objective

To develop and evaluate an adaptive MRI-only workflow for the MR-linac treatment in breast cancer patients eligible for APBI, regional lymph node irradiation or a radiotherapy boost on tumor positive lymph nodes. Furthermore, to investigate whether MRI, in addition to the standard FDG-PET scan and/or RT planning CT scan only, can increase the accuracy in delineation of individual tumor positive lymph nodes in patients with an indication for a RT boost on the involved nodes.

Study design

Prospective imaging study.

Study burden and risks

No risks are expected for patients undergoing MRI given that they will be screened according to the MRI safety criteria. Patients will undergo non-contrast-enhanced MRI(s) of the breast or regional lymph nodes. The time burden consists of one to three imaging procedures on different days, which will each take approximately 30 to 90 minutes.
Patients with tumor positive lymph nodes on standard diagnostic FDG-PET and an indication for RT are selected to undergo an additional RT planning CT scan. Consequently, there will be an additional irradiation load of approximately 3.5-6.0 millisievert (mSv), which involves very low risk for the patient of developing a second malignancy. The time burden of the RT planning CT scan will consist of approximately 15 minutes.
The standard diagnostic FDG-PET scan in supine position will be used for registration, and will not lead to additional risks.
The additional MRI scans (and RT planning CT scan if indicated) will not

interfere with the standard clinical practice and no treatment delay will occur.
For the current patient population, no related benefits are expected. If the study objectives can be achieved, future patients eligible for APBI, regional lymph node RT or a RT boost on tumor positive lymph nodes, will benefit from a non-invasive and shorter RT schedule on the MR-linac instead of surgery.

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

- Female gender;
- *18 years old;
- Patients with cTis-4N0-3M0-1 breast cancer (before any treatment) or with pTis-4N0-3M0-1 breast cancer (postoperatively);

- Written informed consent provided.;Additional inclusion criterion for the MRI regional lymph nodes imaging arm and RT planning CT scan:
- Positive lymph nodes based on standard diagnostic ultrasound-guided fine needle aspiration.
- Tumor positive axillary lymph nodes on standard diagnostic FDG-PET scan:
o For preoperative study participation: on FDG-PET scan before start of any treatment;
o For postoperative study participation: on FDG-PET after neoadjuvant systemic therapy if neoadjuvant systemic therapy was given.

Exclusion criteria

- Legal incapacity;
- MRI exclusion criteria of the MRI safety group of Radiology (UMC Utrecht);
- Previously known inability to undergo the scanning procedure.;Additional exclusion criterion for patients in the regional lymph nodes imaging arm:
- Previous ALND and/or surgery of the supraclavicular region.;Additional exclusion criterion for patients in the breast imaging arm:
- Breast tumor > 3 cm;
- For postoperative study participation: large seroma volume during physical examination and/or on standard RT planning CT.

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):	19-12-2016
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	01-06-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-12-2016
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	18-05-2018
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	NL56683.041.16