First-In Man (FIM) study MR-Linac

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To confirm the pre-clinically demonstrated technical accuracy and safety of the newly developed MR Linac in the clinical setting.

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45369

Source
ToetsingOnline

Brief title
FIM MR-Linac

Condition

- Other condition

Synonym
Bone metastases, cancer

Health condition

Bot metastasen

Research involving
Human

Sponsors and support

Primary sponsor: Elekta
Source(s) of monetary or material Support: ZonMW;STW,KWF/AD6;Zilveren Kruis/Achmea;Elekta;Philips,Philips

Intervention

Keyword: □ Bone metastases, □ First-in-Man study, □ Image Guided Radiotherapy, □ MR-Linac

Outcome measures

Primary outcome

To confirm in the clinical setting:

* Safety of the treatment system

* Geometrical accuracy of real-time targeted irradiation with real-time MR

imaging

Secondary outcome

* Feasibility of the clinical workflow

* Patients (dis)comfort

Study description

Background summary

Image Guided Radiotherapy (IGRT) has become the standard of care to optimize the accuracy of irradiation delivery. To minimize the geometrical uncertainties of the tumor location and shape, in-room image guidance by cone beam CT (CBCT) prior to radiotherapy, has been introduced.

To optimize dose distribution and more precise dose delivery for sparing of the surrounding healthy tissues, accurate tumor localization and tumor shape determination are required. Unfortunately, CBCT has limited soft-tissue contrast, which makes it is difficult to distinguish organs from tumors. A small portion of additional irradiation is necessary for image generation and improved contrast in the CBCT-image. Additionally, real-time anatomical data during irradiation delivery is not possible when CBCT guided therapy is used. Appliance of MRI solves both problems, without delivering an additional radiation dose to the patient, which makes it more attractive for everyday use.

The MR-Linac integrates a radiotherapy accelerator with an MRI with a diagnostic quality of 1.5T, enabling real-time soft-tissue visualization of

human anatomy during radiotherapy. By an improved real-time visualization of the tumor and the surrounding healthy tissues using MRI, it is possible to adapt the dose to the actual anatomy. Thereby, it is possible to provide an increased radiation dose to the tumor, while damage to surrounding organs will be minimized. It is expected that the MR-Linac has a broader therapeutic window as compared to conventional therapy. Additionally, treatment with the MR-Linac has the potential to replace invasive surgery in treating tumors.

When this study confirms that treatment with the MR-Linac is safe, follow-up studies will be set-up to define the applications for which the MR-Linac is suitable.

Study objective

To confirm the pre-clinically demonstrated technical accuracy and safety of the newly developed MR Linac in the clinical setting.

Study design

This is a first-in-man (FIM) study of the MR-Linac, conducted at the UMC Utrecht, to evaluate the clinical safety and accuracy of the MR-Linac in humans. In this study, five (5) patients with bone metastases will be included, who will be treated for pain reduction (palliative policy).

Patients with palliative policy and a signed informed consent to participate in the current PRESENT cohort study (to receive experimental care) and meet the study criteria, will be asked to participate in this study.

When they decide to participate, patients are screened by physical examination and their medical history, such as histological background, to determine malignancy of the metastases. Additionally, a CBCT-scan is retrieved from the patient to set-up an irradiation plan.

When the patient meets the eligibility criteria , the patient has two days to consider participation in this study. At the second visit, patients will receive a simulation MRI, after which they will be treated with the MR-Linac. In case the target moves out of its defined boundaries, through which the irradiation plan is not sufficient, the radiation oncologist and the clinical physicist will evaluate the situation and decide together to restart the whole simulation procedure for treatment with the MR-Linac or cancel the procedure and treat the patient with the conventional Linac.

At the end of treatment, patients will be asked to complete three questions concerning their experience with the MR-Linac treatment, to assess for discomfort of the treatment. Additionally, the radiotherapist will follow up the patients through a phone call. This occurs one day, two weeks, and twelve

weeks after treatment, to assess their health. Thereby, the safety of the treatment with the MR-Linac can be determined.

Intervention

The patient is treated once with a targeted irradiation dose of 8 Gy (8000 msV).

Study burden and risks

There is an increased treatment time with the MR-Linac of 30-60 minutes compared to de regular treatment of 10-15 minutes. Additionally, standard MRI risks apply, such as local heating and claustrophobia.

Patient burden includes an extra hospital visit, an increased treatment time and associated risks with the MR-Linac, and three additional phone calls. Altogether, it may take about 135 minutes of patients time.

Due to the following reasons, the intended study is classified as a low-risk study:
Routine clinical care of bone metastases with the intention to relieve pain of the patient consists of radiotherapy by single beam irradiation with wide safety margins and inhomogeneous dose distribution. In the current study, irradiation is administered with smaller margins and superior dose homogeneity. Eventual positioning errors of up to 5 mm and dose distribution accuracy less than 5% are still considered superior to standard treatment conditions.

In case these margins are exceeded, treatment on the MR Linac is abandoned and the patient will be treated with the conventional Linac. A standard 1.5T MRI is considered safe, and possible related side effects are negligible (see attached folder *MRI* from the department of Radiotherapy, UMC Utrecht). The present 1x8Gy irradiation scheme does not exceed the tolerance dose for any of the proximate normal tissues. In order to detect adverse events, follow-up will be performed at day 1 after treatment, at 2 weeks and at 3 months by telephone or by hospital visit on indication. Then, questions concerning patient health will be asked, to determine safety of the treatment by the MR-Linac. Patient health or morbidity will be assessed according to the presence or absence of symptoms such as nausea, pain and fatigue, specific for the treated anatomic region.

Independent from the MR-Linac development, patients are currently already safely being treated by other technologies based on MR-guided radiotherapy in other centers (such as radiotherapy using cobalt sources and 0.35T MRI).

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

* Painful bone metastases in the lumbar spine
* Radiographic evidence of bone metastases
* Histologic proof of malignancy
* Karnofsky Performance Score * 50
* Age * 18 years
* Able to provide a written informed consent

Exclusion criteria

* Prior radiation therapy within the region planned to be irradiated
* Contraindication for MRI according to screening protocol radiology department UMCU (e.g.

cardiac pacemakers, and defibrillators, artificial heart valves or cochlear implants, https://richtlijn.mijnumc.nl/Beeld/MRI/Paginas/MRI-Veiligheid-Contra-indicaties.aspx
* Claustrophobia
* Standard chemotherapy or radionuclide therapy within 48 hours before or after treatment
* Any other type of systemic anti-cancer treatment, except for endocrine treatment
* Unstable spine requiring surgical stabilization
* Neurological deficit
* Not able to provide a written informed consent

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-05-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

Generic name:	MR-Linac
Registration:	No

Ethics review

Approved WMO

Date:	12-04-2017
Application type:	First submission
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	NL60984.041.17

Study results

Date completed: 15-11-2017

Results posted: 13-02-2018

Actual enrolment: 5

First publication
22-01-2018