Precision Radiation treatment for Epilepsy

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Objectives: Primary: to determine whether SRT reduces the seizure frequency resulting in a reduction of at least 75% (RAEC I-III) in patients with drug-resistant focal epilepsy when compared to standard of care. Secondary: Assess quality of life (...

Ethical review	Not approved
Status	Will not start
Health condition type	Seizures (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON51868

Source
ToetsingOnline

Brief title
PRECISION

Condition

- Seizures (incl subtypes)

Synonym
epilepsy, seizure

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic
Source(s) of monetary or material Support: ZonMW / Zorginstituut

Intervention

Keyword: curative, epilepsy, non-invasive, radiation

Outcome measures

Primary outcome

Main study parameters/endpoints: Primary endpoint: RAEC I - III after 2 year of follow-up.

Secondary outcome

Secondary endpoints: Seizure frequency, Type epilepsy, Seizure-free days, Quality-of-Life in Epilepsy (EQ-5D 5 Level, AQOL-8D, QOLIE-31), Serious Adverse Events (SAE), anti-epileptic drug use, Cost-effectiveness Resource use iMTA Productivity Cost Questionnaire (iPCQ), iMTA Medical Consumption Questionnaire (iMCQ), iMTA Valuation of Informal Care Questionnaire (iVICQ)], Patient-reported outcome measures (PROMs), Patient-reported experience measures *medische specialistische zorg* (PREM MSZ), neuro-cognition.

Study description

Background summary

Rationale: The PRECISION-study offers a non-invasive, curative intervention for patients with drug-resistant focal epilepsy who are not eligible for open brainsurgery. The intervention will consist of a single LINAC-based stereotactic radiotherapy (SRT) treatment and is given by the radiation-oncologist after detailed localisation of the epileptogenic zone (EZ) by the neurologist, radiologist and neurosurgeon. This intervention is not yet available and reimbursed in The Netherlands and will offer the selected patient, who otherwise would be treated with palliative therapy, a non-invasive curative treatment option as a non-competitive alternative to epilepsy surgery. It is expected that the health costs for this curative treatment will not exceed standard treatment, such as lifelong medication and neuromodulation. We hypothesize that: SRT is a superior treatment option compared to palliative

standard of care (i.e. anti-epileptic drugs (AED's) and neuromodulation), for patients with drug-resistant focal epilepsy, not eligible for open surgery, which will result in a higher reduction of seizures (with 50% of the patients reaching a 75% reduction at 2 years).

Study objective

Objectives: Primary: to determine whether SRT reduces the seizure frequency resulting in a reduction of at least 75% (RAEC I-III) in patients with drug-resistant focal epilepsy when compared to standard of care. Secondary: Assess quality of life (QoL) after SRT, define safety, (serious) adverse effects, AED use and tolerability of SRT, investigate the cost-effectiveness (CEA) of SRT compared to standard of care.

Study design

Study design: Randomised controlled trial in which SRT is the intervention and AED continuation and neuromodulation are the standard treatment with a 1:1 randomization to firmly establish QoL and CEA. Randomisation will be based on block randomisation with variable block size of 2, 4 and 6.

Intervention

Intervention: LINAC-based Stereotactic Radiotherapy (SRT): Target definition: the target volume is defined as the epileptogenic zone (EZ) on all (non) invasive examinations of the presurgical trajectory. A single fraction SRT with a prescribed isotoxic dose of 24 Gy to the 100% surrounding isodose.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: There is currently in the Netherlands no non-invasive, curative intent treatment for adult/pediatric patients with drug-resistant, focal epilepsy, who are not eligible for surgery, therefore there is an unmet need for the innovative treatment that the PRECISION-trial will provide. SRT for epilepsy is already applied in neighboring European countries (e.g. France, Belgium and Germany), the USA, China and Japan with reported effectiveness is 58% post-treatment satisfactory seizure outcome (RAEC scale I + II = no to rare seizures) at 2 years follow-up.

The risks of the SRT treatment are based on the location of the EZ zone. Information is available in the literature on the risks of treating patients with epilepsy, brain metastases or benign brain lesions.

The most common acute adverse reaction of SRT is headache, nausea and/or vomiting caused by reversible intracranial edema and can be treated with

corticosteroids. Long-term side effects include transient neurologic deficits and seizure exacerbation, changes in mMagnetic resonance imaging (MRI), expected and usually asymptomatic superior quadrantanopia (for lesions treated in the temporal lobe), ischemic events, cognitive changes, and radiation necrosis rarely leading to symptomatic edema or cysts requiring surgical intervention.

If the EZ zone is close to the pituitary, potential risks can be estimated based on the literature on the management of patients with pituitary tumors. Cerebral infarction has been described as a long-term complication of stereotactic radiotherapy of benign skull base tumors, mainly pituitary tumors (SIR 1.48 - 4.2). When treating the amygdala, patients may face a similar risk due to its close relationship with the internal carotid artery].

In patients with a pituitary adenoma, it is known that hypopituitarism can occur after conventional and stereotactic radiotherapy in 50% of patients, 10 years after treatment. However, in patients with a non-functional pituitary adenoma population in 37-85% of patients already have hypopituitarism at the time of diagnosis. Hormone production deficiency after conventional radiotherapy of the pituitary gland with 45Gy is 45-100% for GH, 18-30% for LH/FSH, 15-22% for ACTH and 25% for TSH.

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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

1. Age >= 18 years, non-pregnant, written informed consent
2. The patient or caretaker is able to keep an epilepsy diary
3. The patient has a diagnosis of epilepsy established by a dedicated neurologist
4. The patient had at least 3 focal-onset seizures with impairment of consciousness over a 3-month period despite two or more antiepileptic medication trials (according ILAE Task Force on therapeutic strategies)
5. Video electroencephalography to determine a well-circumscribed seizure focus
6. Imaging evidence (i.e. 3T-MRI) of the anatomic region to be targeted with SRT, correlating with the EZ hypothesis
7. A Wada test or a functional MRI to lateralize language has been performed in selected patients
8. The patient has completed a standard battery of neuropsychological testing
9. The patient been deemed an appropriate candidate for stereotactic radiosurgery by a dedicated Radiation Oncologist and Neurosurgeon and referred for the study by one of the Dutch regional multidisciplinary epilepsy surgery working groups
10. Patients that were rejected for surgery in an earlier stage can participate in the trial if the treatment with VNS/DBS was more than 4 years ago.

Exclusion criteria

1. If a radiation treatment plan with a V12Gy <= 10 cc in healthy brain is not feasible.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	94
Type:	Anticipated

Ethics review

Not approved

Date:	23-01-2023
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
Other	NCT05182437
CCMO	NL81166.068.22