Focal Cortical Dysplasias and Epilepsy: Characteristics of Histopathology and 7 tesla MRI.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms benign
Study type	Observational invasive

Summary

ID

NL-OMON44372

Source
ToetsingOnline

Brief title
CODE 7

Condition

- Nervous system neoplasms benign
- Congenital and peripartum neurological conditions
- Nervous system, skull and spine therapeutic procedures

Synonym
epilepsy, epileptic seizures

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Nederlands Epilepsiefonds

Intervention

Keyword: 7 tesla, Dysplasia, Epilepsy, magnetic resonance imaging

Outcome measures

Primary outcome

• Presence on 7T MRI and lower-field MRI of specific characteristics of FCD.

Comparison of imaging characteristics on 3 and 7 T MRI.

• Correlates between in-vivo and ex-vivo 7 T MRI characteristics and

histopathological findings and quantifications in resected dysplastic tissues.

• Histopathological diagnosis

Secondary outcome

• Seizure outcome

• Seizure frequency

• Semiology

• Age of seizure onset

• Abnormalities on PET

• Abnormalities on SPECT

• Abnormalities on MEG

• Abnormalities on EEG

• Abnormalities on Electrocorticography

Study description

Background summary

Focal Cortical Dysplasia (FCD) is a developmental brain abnormality and one of the most common causes of therapy resistant epilepsy. Hallmarks of FCD are disrupted cortical layering and immature and dysmorphic neurons. Neuronal function in FCD lesions is disrupted and has a lower seizure threshold than normal brain tissues or can even produce constant or periodic epileptic discharges.
Anti-epileptic medication does not effectively control seizure activity in 76% of patients with FCD. Over the last decennia epilepsy surgery has been quickly gaining ground as therapy for epilepsy. If possible to identify a circumscript epileptic focus, resective surgery has a high chance (up to 80%) of achieving seizure freedom, in case of incomplete resection, i.e. in cases where the lesion could not be well identified in imaging or where the epileptogenic lesion is located in or near eloquent regions, this is only around 20%.
Surgery is so far the only curative treatment for epilepsy. Identification of a resectable lesion in patients with epilepsy remains a challenge, especially when a focal developmental malformation is suspected. Absence of a lesion on MRI has been shown to be a predictor of poor surgical outcome and necessitates additional diagnostic tests. In MRI-negative patients that are operated, Focal Cortical Dysplasia (FCD) is reported in up to 60%. In 36% of patients FCD MRI does not show a lesion.
Advances in imaging techniques are expected to improve the detection of epileptogenic lesions and could consequently increase the portion of epilepsy patients eligible for surgery and improve the results of surgical intervention. Advantages of 7 tesla MRI over lower-field systems are the higher signal-to-noise ratio that allows increased spatial resolution and, and therefore potentially has a higher sensitivity for subtle structural abnormalities However, the clinical merit of 7 tesla MRI has not yet been scientifically proven for patients with epilepsy.

Study objective

In this study one of the goals is to compare 7 tesla MRI with 3 tesla MRI in terms of lesion detection in epilepsy patients and depiction of specific dysplasia-related imaging characteristics. Furthermore, resected tissue will be scanned ex-vivo at 7 tesla. The extremely high resolution images created will be compared with histopathological measures of cellular and neuronal density, myelinisation and inflammation among others. This will provide a better understanding of the structural and histopathological substrate for specific MRI characteristics. In turn these data can form the basis for defining additional identifying characteristics and the development of improvements in imaging for epileptogenic lesions.

Study design

This study is a single center observational study. The duration of the study is expected to be two years. The study will be performed in the department of

Neurology and Neurosurgery of the UMC Utrecht, in collaboration with de department of Radiology UMC Utrecht (especially the 7 tesla MR group), department of pathology UMC Utrecht. Patients will receive the normal work-up for the epilepsy surgery program with as addition an extra 7 T MRI. Some patients already had clinically indicated 7T MRI. These scans were carried out according to scanning protocols that are the same as used in this study. These patients can be enrolled in the study without the need to repeat the 7T MRI.
If it leads to resective surgery, the tissue will be scanned ex-vivo at 7 tesla prior to the histopathological examination. On top of the routine histopathological diagnostics, extra techniques will be used to further characterize lesions. This has no consequence for the routine clinical histopathological examination

Study burden and risks

Epilepsy caused by the developmental abnormalities typically presents at child-age, consequently minors make up the largest group of potential candidates for epilepsy surgery. Histopathological diagnoses of developmental abnormalities - including FCD - are predominantly found in infant and juvenile patients. Excluding patients of child age would form a study group not representable for patients with developmental brain abnormalities.
To date no permanent negative health effects of MR imaging have been reported, after millions of MRI scans, including an appreciable number at field strengths of 7 tesla and higher. Compared to scanning with 1.5 or 3 T systems (the current clinical standard) no increase in health risk should be expected with scanning at 7 Tesla, since it adheres to the same limitations of Specific Absorption Rate (SAR). Accordingly, in 2003 the FDA concluded that in adults, children and infants aged>1 month MRI up to field strengths of 8 tesla holds no significant risk. However, scanning at higher field strength may be experienced as more unpleasant due to higher noise levels, the longer and narrower bore and occurrence of potentially unpleasant physical sensations, such as nausea, vertigo, tingling and twitches. Nonetheless, 7 T MRI is well tolerated, and scores of discomfort are very close to those of 3 T MRI.
The added burden of participation in the study is solely by the addition of the 7 T MRI in a diagnostic trajectory of several investigations, including 3 T MRI, EEG, and one or more of the following: PET, MEG, and SPECT. This burden can be considered acceptable because 7 T MRI is potentially able to visualize abnormalities which are not, or partially, detected using other diagnostic tools. This extra information could mean that a better surgical plan can be made, with more chance of complete resection and thus with a bigger chance of seizure freedom. Some patients in whom surgery was not considered possible may even become surgical candidates.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1. All patients selected by the Dutch Collaborative Epilepsy Surgery Program board for the diagnostic work-up for the surgical treatment of refractory epilepsy and a suspected malformation of cortical development or cortical dysplasia as underlying cause, with and without presence of primary lesion (mesiotemporal sclerosis, glioneuronal tumor, vascular malformation or traumatic brain injury at young age). Also, in case of suspicion of focal epilepsy and negative clinical (3T) MRI
2. Prior clinical 1.5 or 3T MRI

Exclusion criteria

1. Age under 6
2. Mentally or physically incapable of giving consent (for age 12 years and up)
3.Insufficient understanding of Dutch written or spoken patient information (parent or legal guardian for patients under 12, both patient and parent or legal guardian for patients in the age 12-18)
4. Uncooperative during previous MRI scans
5. Contra-indications for 7 T MRI as specified by the UMCU radiology department at the time of inclusion.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-08-2015
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	14-04-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	06-10-2015
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	23-02-2016
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	NL48069.041.14