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A randomised control trial of SEEG electrode placement methods

Submission date
14/11/2016

Recruitment status
No longer recruiting

Registration date
15/11/2016

Overall study status
Completed

Last Edited
14/10/2022

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Epilepsy is a condition that affects the brain, which causes a person to experience seizures. It is estimated 1% of the population suffer from epilepsy and between 30-40% of these patients are unable to control their seizures despite trying two or more anti-epileptic drugs (drug refractory focal epilepsy). Surgical treatment can offer a potential cure for these patients. In order to find out if a patient is suitable to undergo surgery, they need to undergo a specialist evaluation to find the part of the brain that is causing the problem. In almost half of patients, performing non-invasive procedures such as brain scans are not enough to find the route of the problem, and so it is necessary to place electrodes (electrical conductors used to measure electrical activity) directly onto the exposed surface of the brain (Stereotactic EEG (SEEG) or depth electrodes). SEEGs carry a number of risks, including bleeding, infection and damage to important brain structures if they are misplaced. The accurate placing of depth electrodes is therefore very important. The iSYS1 trajectory guidance system is a small robotic device that has been developed to improve the accuracy of depth electrode placement. The aim of this study is to investigate the use of the iSYS1 trajectory guidance system compared to the standard technique.

Who can participate?
Adults with drug refractory focal epilepsy who require a SEEG as part of routine clinical care

What does the study involve?
Participants who are having a SEEG as part of their normal care are randomly allocated to one of two groups. Those in the first group have the depth electrodes placed using the usual mechanical arm technique. This involves the use of a neuro-navigation system and the surgeon aligning a mechanical arm along a pre-planned trajectory (route). Once the trajectory has been lined up, a cut is made in the skin and a small hole is drilled through the skull. A metal bolt is then screwed into the skull through which the electrode is inserted along a premeasured length to reach the target in the brain. The electrode is then secured in place by the bolt. Those in the second group have the depth electrodes placed using the iSYS1 trajectory guidance system. This involves the use of a neuro-navigation system relaying the plan information to a small guidance system that the surgeon places a few centimetres from the surface of the scalp. The guidance system, through a series of small steps then aligns to the pre-planned trajectory with a high level of accuracy. Once the trajectory has been lined up, a cut is made in the skin and a small hole is

drilled through the skull. A metal bolt is then screwed into the skull through which the electrode is inserted along a premeasured length to reach the target in the brain. The electrode is then secured in place by the bolt. The time taken for the electrodes to be placed in both groups is measured during the surgery. 48 hours after surgery, participants then undergo a brain scan to see how accurately the electrodes have been placed and check for any complications such as bleeding.

What are the possible benefits and risks of participating?
There are no direct benefits or risks involved with participating.

Where is the study run from?
National Hospital for Neurology and Neurosurgery (UK)

When is the study starting and how long is it expected to run for?
January 2015 to January 2018

Who is funding the study?
Wellcome Trust (Grant number: WT106882) (UK)

Who is the main contact?
Professor John Duncan
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16/0590

Study information

Scientific Title
Single-blinded randomised case control parallel group single-site investigation of stereoencephalography electrode placement in patients with refractory focal epilepsy

Study objectives
The use of the iSYS1 trajectory guidance system (Medizintechnik GmbH) in comparison to the conventional mechanical arm based technique (using the precision aiming device) will:
1. Reduce the operative time taken for target alignment and electrode insertion
2. Improve the accuracy of bolt entry point position at the skull compared to the pre-operative plan
3. Improve the accuracy of electrode target point position compared to the pre-operative plan
4. Improve accuracy of angle of bolt insertion at the skull compared to the pre-operative plan
5. No increase in clinically significant and non-clinically significant radiological post-operative haemorrhage rate
6. No increase in infection rate
7. No increase in new post-operative neurological deficits

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/02/2017, Health Research Authority, REC ref: 17/EE/0016, MHRA ref: CI/2017/0026.

Study design
Single-blinded randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
See additional files

Health condition(s) or problem(s) studied
Drug resistant focal epilepsy

Interventions
Patients who are scheduled for SEEG implantation as part of their routince medical care will be invited to take part in the study and are randomised by an independent statistician through the use of a computer generated system that contains a code assigning the patient to receive the current gold-standard method of implantation using the mechanical arm based technique (Precision-aiming device) or the robotic trajectory guidance system (iSYS1).

Group 1: Participants undergo surgery with the currently used mechanical arm based technique (using the precision aiming device) to place electrodes. The manual technique of SEEG placement involves the use of a neuronavigation system and the surgeon aligning a mechanical arm along a pre-planned trajectory. Once the trajectory has been aligned a skin incision is performed and a small hole is drilled through the skull. A metal bolt is then screwed into the skull through which the electrode is inserted along a premeasured length to reach the target in the brain. The electrode is then secured in place by the bolt.

Group 2: The iSYS1 trajectory guidance system (Medizintechnik GmbH) for aligning the trajectory of the electrodes to be placed. The iSYS1 trajectory guidance system technique of SEEG placement involves the use of a neuronavigation system relaying the plan information to a small guidance system that the surgeon places a few centimetres from the surface of the scalp and the guidance system, through a series of small steps will then align to the pre-planned trajectory with a high level of accuracy. Once the trajectory has been aligned a skin incision is then performed and a small hole is drilled through the skull. A metal bolt is then screwed into the skull through which the electrode is inserted along a premeasured length to reach the target in the brain. The electrode is then secured in place by the bolt.

Total duration of treatment is 3-4 hours for the SEEG surgery. Surgical implantation time will be measured during the surgery. Follow up will be in the form of a post-operative CT and MRI scan within 48 hours of surgery from which the accuracy data and complications (haemorrhage) will be determined. All other measures will be collected as part of ‘routine care’ and will not fall within the trial duration.

Intervention Type
Device

Phase
Phase III

Primary outcome measure
Surgical implantation time will be measured in minutes and seconds during surgery.

Secondary outcome measures
1. Accuracy of SEEG depth electrode placement, as assessed by skull entry point (mm), error of angle (degrees) of implantation of intracranial bolt and target point error (mm) of the actual electrode tip compared to the planned target point as defined by the preoperative plan and target region sampled, as lateral deviation measured by the research team from the CT/MRI scan following surgery
2. Incidence of clinically significant and non-clinically significant radiologically detected post-operative haemorrhages (%) is measured using post-operative imaging within 48 hours of implantation
3. Infection rate (%) is measured by the presence or absence of infection on clinical observation and corroborated by blood test markers of infection such as white cell count and C-reactive

protein as appropriate by the clinical team at routine follow up or medical note review if the patient asks medical assessment prior to the routine follow up period.
4. New post-operative neurological deficits (%) are measured by the presence or absence of a new neurological deficit on clinical observation by clinical team at routine follow up
5. Operator (surgeon) based opinions for ease of use and perceived safety of the iSYS1 trajectory guidance system compared to conventional mechanical arm based insertion is measured by documenting comments at the end of each operation on the electronic clinical research form (eCRF).
6. Proportion of patients that are offered resective surgery and seizure freedom following resective surgery (if performed) is measured by medical note review at routine follow up
7. Number and nature of adverse events is measured by the medical note review by the clinical team at routine follow up

Overall study start date
09/01/2015

Completion date
31/05/2019

Eligibility

Key inclusion criteria
1. Age 18-80 years
2. Drug refractory focal epilepsy
3. Deemed to require SEEG placement as part of routine clinical care following multidisciplinary team meeting decision
4. Informed consent from patient to undergo intracranial SEEG investigation as part of routine clinical care

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
32 (16 in each arm)

Total final enrolment
32

Key exclusion criteria
1. Pregnancy
2. Uncorrectable coagulopathy
3. Lacking capacity to consent

Date of first enrolment
01/02/2017

Date of final enrolment
01/10/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
National Hospital for Neurology and Neurosurgery
Queen Square
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Sponsor information

Organisation
University College London

Sponsor details
Joint Research Office
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Sponsor type
University/education

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Research organisation

Funder Name
Wellcome Trust (Grant number: WT106882)

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
After completion of the study the results will be submitted for publication to an established peer reviewed journal and the data will also be presented at scientific forums/meetings. All proposed publications will be discussed with and reviewed by the Sponsor prior to publishing other than those presented at scientific forums/meetings.

Intention to publish date
31/12/2019

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository, the UCL Data Repository. Requests for patient-level data and statistical code should be made to the corresponding author and will be considered by members of the original trial management group, including the chief investigator and members of the University Joint Research Office, who will release data on a case by case basis. Data will be shared following the principles for sharing patient-level data as described by Tudur Smith et al (BMC Medicine 2015; 13: 298). The data will not contain any direct identifiers, the researchers will minimise indirect identifiers, and remove free text data to minimize the risk of identification.

IPD sharing plan summary
Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1	14/11/2016	15/11/2016	No	Yes

Results article	results	24/08/2021	26/08/2021	Yes	No
Protocol file	version 3.0	03/07/2017	14/10/2022	No	No
HRA research summary			28/06/2023	No	No