Validation of the mjn-SERAS medical device for the early detection of epileptic seizures in refractory epilepsy patients in a normalised environment: Protocol for a prospective, multicentre, controlled and randomized, pilot clinical study

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Abstract

Background: Approximately one third of epilepsy patients are resistant to anti-seizure medication (ASM). There are currently no mobile devices that allow early detection of seizures. Hypothesized that the use of an intra-aural EEG device (mjn-SERAS) will allow the activity recording and the subsequent processing by the AI algorithm of MJN to anticipate the event of suffering an epileptic seizure in those patients already diagnosed previously, generating an alert to prevent accidents.

Objective: To assess the epilepsy-related quality of life in patients with drug-resistant epilepsy using the mjn-SERAS solution compared to the control group
To assess the seizure-related safety in patients with drug-resistant epilepsy using the mjn-SERAS solution compared to the control group in terms of the number of accidents caused by seizure episodes

Methods: A prospective, multicentre, pilot clinical trial, with a controlled and randomized design, is proposed to validate a medical device (mjn-SERAS), CE certificated. This new validation will be in the participant's normalized environment, in individuals over 2 years of age, with a diagnosis of refractory epilepsy, which will make it possible to determine the impact of the mjn-SERAS device on the early detection of epileptic seizures and the generation of a pre-seizure alert with a time window of a minimum of 1 minute. The sample size determined is an n=150 exposed individuals who meet the inclusion criteria. The sensitivity, specificity, positive predictive value, PPV and F-Score of the device will be analysed. Also, the degree of satisfaction of patients and their caregivers, including the impact on quality of life and the degree of health perceived by the caregiver when alarms are generated to assess the possibility of a new epileptic seizure. Finally, to describe possible improvements in indicators of social relationships in different areas of personal development.

Results: This study is funded in 2022 by the EIT Health and European Union, under the programme EIT Health Amplifier n. 220445-230126.
As of February 2025, we enrolled 76 patients in 6 clinical sites in Spain, UK and Germany. Data analysis is currently underway, and the first results are expected for June 2025.

Conclusions: The mjn-SERAS device, an intra-aural EEG, aims to record brain activity and use artificial intelligence (AI) algorithms to anticipate seizures in previously diagnosed patients. By generating early alerts, it allows individuals to take

preventive measures and enhance safety. Although participants may not experience direct benefits, validating or improving this technology could enhance future epilepsy management and treatment.
Unlike previous research efforts, mjn-SERAS is the first device to systematically provide seizure alerts using an AI-based algorithm to detect early warning signs. Its real-world application could significantly improve the quality of life for epilepsy patients and advance medical understanding of seizure prediction.
This study evaluates the device's accuracy in predicting seizures in everyday settings and assesses its psychological, mental, and social impact on people with refractory epilepsy. Clinical Trial: ClinicalTrials.gov NCT05845255; https://clinicaltrials.gov/study/NCT05845255

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ABSTRACT

Background

Approximately one third of epilepsy patients are resistant to anti-seizure medication (ASM). There are currently no mobile devices that allow early detection of seizures. Hypothesized that the use of an intra-aural EEG device (mjn-SERAS) will allow the activity recording and the subsequent processing by the AI algorithm of MJN to anticipate the event of suffering an epileptic seizure in those patients already diagnosed previously, generating an alert to prevent accidents.

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Ethical considerations :

This study is approved by an accredited Drug Research Ethics Committee (CEIm); specifically, by the Regional Drug Research Ethics

Committee of the Community of Madrid in Spain. Subsequently approved by Wales Research Ethics Committee 4, Wrexham for Oxford in UK and Ethik-Kommission Universität Freiburg for Kork in Germany. All patients have an informed consent with the information of the study and the option to go out in any moment. The study is pseudonimized with the hospitals, they have the ability to recover all patients data, but the sponsor and all collaborators have all data completely anonymized. There is no economic compensation for the participants.

Results

This study is funded in 2022 by the EIT Health and European Union, under the programme EIT Health Amplifier n. 220445-230126.
As of February 2025, we enrolled 76 patients in 6 clinical sites in Spain, UK and Germany. Data analysis is currently underway, and the first results are expected for June 2025.

Conclusions

The mjn-SERAS device, an intra-aural EEG, aims to record brain activity and use artificial intelligence (AI) algorithms to anticipate seizures in previously diagnosed patients. By generating early alerts, it allows individuals to take preventive measures and enhance safety. Although participants may not experience direct benefits, validating or improving this technology could enhance future epilepsy management and treatment.
Unlike previous research efforts, mjn-SERAS is the first device to systematically provide seizure alerts using an AI-based algorithm to detect early warning signs. Its real-world application could significantly improve the quality of life for epilepsy patients and advance medical understanding of seizure prediction.
This study evaluates the device's accuracy in predicting seizures in everyday settings and assesses its psychological, mental, and social impact on people with refractory epilepsy.

REGISTRATION

ClinicalTrials.gov NCT05845255; https://clinicaltrials.gov/study/NCT05845255

INTRODUCTION

Background and rationale

The International League Against Epilepsy (ILAE) describes a seizure as the transient appearance of signs and/or symptoms due to excessive or synchronous abnormal neuronal activity in the brain, in addition, epilepsy is defined as a disorder of the brain characterized by an enduring predisposition to seizures and by the neurobiological, cognitive, psychological and social consequences of this condition; the diagnosis of epilepsy requires the occurrence of at least one epileptic seizure [1]. The World Health Organization estimated in 2019 that around 50 million people worldwide were diagnosed with epilepsy, which develops at any age with a higher incidence in the youngest and in the elderly and entails an increased risk of premature death of up to three times in patients compared to the general population[2]. Epilepsy is considered a multifactorial disease with a wide spectrum of characteristics and different predisposing factors for its development, the consequences include not only the impact in the patient's health, but also all aspects (cultural, interpersonal and social) of a person's life[3]. Around 70% of epilepsy patients could live without suffering from seizures in spite of an accurate diagnosis and treatment. Therefore, the main purpose of epilepsy treatment is to diminish seizures to a minimum level that allows patients to achieve the best possible quality of life[4]. Although most patients remain seizure-free with anti-seizure medication (ASM), more than 30% continue to have seizures despite treatment. This situation is known as drug-resistant epilepsy or refractory epilepsy[5,6] and is associated with a greater socioeconomic and psychosocial burden[7,8]. The random and unpredictable nature of seizures is one of the principal factors affecting the patients quality of life[9,10], along with associated-comorbidities, neuropsychiatric disorders, cognitive deficits and side effects of ASM [2]. Therefore, there is an urgent need to develop reliable tools for accurate seizure prediction and early detection, that is defined as the programmed recognition of oncoming seizures, before they initiate primarily, usually within a time period of a few minutes[11]. In this regard, it is known that EEG is a valuable non-invasive method of diagnosis in epilepsy that can display abnormalities in brain activity, disrupted EEG features enable classification, localization and rise the likelihood for seizure detection, therefore, it could potentially assess seizure recurrence risk [12]. However, the diagnosis of epilepsy is also centred on clinical information and the EEG should be considered as support but not an exclusive diagnostic test[13], On the other hand, prolonged video-EEG monitoring, by analysing both EEG and ictal semiology of seizures, often yields the confirmatory diagnosis [14,15]. Video-EEG monitoring remains the gold standard of epilepsy for the detection and diagnostic evaluation of seizures in clinical practice, however this method has a limited sensitivity, requires long time for analysis, and is subject to different interobserver and intraobserver biases[16]. Because of this there is a need to develop robust seizure detection methods that allow a higher sensitivity and are more instrumental. New computer-based technology has improved the quality of EEG assessments[17] and open a road for EEG machine learning-based prediction. These algorithms can be trained to learn patterns from a big data base by processing it throughout a multi-layer hierarchical architecture, allow seizure detection and they might provide warnings to patients in the near future, allowing for acute treatment at the time of seizure onset[18,19].

MJN Neuroserveis (hereinafter MJN and/or Sponsor) is a company composed of a team of researchers and engineers that has developed mjn-SERAS, a wearable technology to assess the likelihood of the presentation, manifestation or occurrence of epileptic seizures. MJN aims to redefine the concept of seizure detection using artificial intelligence technology to improve people's quality of life. It has been working intensively on the development of algorithms for years to assess the likelihood of epileptic seizures using artificial intelligence tools, this solution is disruptive due to epilepsy being medically defined as unpredictable.

Following the launch of an initial study to validate the performance of the MJN artificial intelligence algorithm to detect and predict changes in the EEG graph elements of patients in the Episoft study and the subsequent design and execution of the SERAS-EEG study with the aim of analysing and validating the performance of the mjn-SERAS intra-atrial device versus the "gold-standard" video-EEG (hereinafter v-EEG) as a valid system for the evaluation of the concordance and prediction of the likelihood of epileptic seizures taking place in clinically diagnosed patients, it can be established as a valid preclinical alarm signal against the onset of epileptic seizures. Once the two previous validations, fundamental to establishing the functioning and use of the mjn-SERAS intra-atrial device, have taken place, we now face the greatest challenge of the project: validating the operation of our mjn-SERAS device in day-to-day activities of the patient, i.e., to validate its operation when worn by the patient at home, at school, at work, etc. This is undoubtedly the biggest challenge, since we are leaving behind the predictable and controlled environments of the hospital site for environments with many external factors that are difficult to control. Research with a clearly personalised component in each participating subject, with special emphasis on the different seizure semiology suffered by the different participating subjects with focal epilepsy, and which will also be the subject of future research.

We are proposing the prospective analysis of 150 subjects with a clinical diagnosis of epilepsy whose clinical semiology of their epilepsy is considered to be of interest for the validation of this study. This will allow the validation of the correlation and operation of the electroencephalographic recording of the mjn-SERAS in the normalised environment of the patient as well as the analysis and reliability of the assessment alert s of the possibility of epileptic seizures generated by the mjn-SERAS device during its usual activity. From a methodological point of view, which will be detailed more specifically below, the general clinical variables to be included are the number of seizures (determining the onset of the seizure according to medical criteria), the type of seizure, semiological characteristics, duration, identification of the lateralisation of the epileptic focus, type of epilepsy, etiology and pharmacological resistance. The patient will also be asked to report all the alarms and seizures using a simple app on his/her mobile phone in order to subsequently analyse and determine the results according to the patient's own experience. The validation of the mjn-SERAS intra-atrial device in a standardised patient environment will provide an objective system for the early detection of these

comorbid events prior to their clinical manifestation, a pioneer in current scientific knowledge.

Patient advocacy groups have been involved in the recruitment, participation and dissemination of the study.

Primary hypothesis

- Patients with drug-resistant epilepsy using the mjn-SERAS solution will improve the epilepsy-related quality-of-life compared to the control group when assessed at the post-measurement timepoint.
- The predictive capability of the mjn-SERAS solution to alert users before seizures will reduce the number of accidents in patients with drug-resistant epilepsy compared to the control group between baseline and post-measurement timepoint.

Primary objectives

1.-To assess the **epilepsy-related quality of life** in patients with drug-resistant epilepsy using the mjn-SERAS solution compared to the control group

- **Endpoint**: Change in the epilepsy-related quality of life at T3 compared to baseline in each group (intervention and control).
- **Evaluation**:
  - QOLIE-31 for adults (18 to 65 years) in Spain, UK and Germany
  - QOLIE-AD-48 for adolescents (12 to 17 years) in Spain, UK and Germany

2.- To assess the **seizure-related safety** in patients with drug-resistant epilepsy using the mjn-SERAS solution compared to the control group in terms of the number of accidents caused by seizure episodes.

- **Endpoint**: Change from baseline in the **number of accidents** caused by seizure episodes in T2 period in each group (intervention and control), assessed in T3 period including pre-post-assessment.
- **Evaluation**:
  - Number of accidents caused by seizure episodes counted from the patient-reported entries in the digital diary.

METHODS

Study design

A prospective, multicentre, controlled and randomized pilot clinical study postmarked is proposed to validate a medical device (mjn-SERAS device), which has already been validated and certified in Europe by BSI Group (CE2797) notified body with CE 777314 under MDR, this new validation will take place in the participant's normalised environment, in individuals between 2 and 65 years of age, of both sexes with a diagnosis of refractory epilepsy, according to inclusion and exclusion criteria (Table 1) and CE mark considerations for intended use, which will make it possible to determine the impact of the mjn-SERAS device on the early detection of epileptic seizures and the generation of a pre-seizure alert with a time window of a minimum of 1 and a maximum of 15 minutes. The sensitivity and specificity of the device in the studied environment will also be calculated. The sample size determined is an n=150 exposed individuals who meet the inclusion criteria.

The method applied during the study consists of using a mjn-SERAS device, with the earpiece of the external auditory canal customised for the patient. Once the customised earpiece and device has been designed, the artificial intelligence algorithm will be trained with the information on patient brain activity, by training with new recordings taking place on the same patient with the final device, which will only perform recording functions during the initial weeks to detect brain electrical activity and seizures, which will allow training, testing and optimisation of the algorithm according to study variables (Table 2).

Once the individualised artificial intelligence algorithm has been obtained, the mjn-SERAS device will go into seizure risk alert generation mode, i.e., early seizure detection mode, generating an alarm on the mobile phone that accompanies the mjn-SERAS device, which will inform the patient of the risk situation. The mobile phone application will then "ask" the participant, after a certain period of time, if they have had an epileptic seizure and, if so, the clinical characteristics of the seizure. This information will be collected for the subsequent analysis of the operation of the mjn-SERAS device, as well as the mobile phone application that accompanies the system.

Eligibility criteria

Table 1. Inclusion and exclusion criteria

Inclusion criteria
▪ Age since 2 years to 65 years of age. ▪ Confirmed diagnosis of drug-resistant epilepsy, with focal, generalized or focal -generalized seizures, according to international standards from ILAE 2017 classification, who will be evaluated by a specialised epilepsy unit and who are expected to have seizures. ▪ The video-EEG records of patients must have epileptic seizures counted and recorded by specialised clinical personnel through accepted and contrasted gold-standard systems or evaluated by a specialized epilepsy unit and expected to experience seizures with electroclinical manifestations If there are clear clinical epileptic seizures (e.g. motor seizures), patients could be involved even without v-EEG records, according to medical criteria. ▪ Patients with a clinical history and previous video-EEG records that allows certainty about the diagnosis and characteristics of the participant’s epilepsy. If there are clear clinical epileptic seizures (e.g. motor seizures), patients could be involved even without v-EEG records, according to medical criteria. ▪ Precise semiological information on the patients included. ▪ Patients with both sides localisation will be accepted, and the wearable device will be placed in the side that is most evident the origin of the seizures, to be placed as near as possible to the focal point. ▪ Presence of more than 10 day seizures per year, from tonic, tonic-clonic, clonic or atonic seizures, and a minimum of 2 to 4 day seizures per month (preferably 4 per month/ 1 per week) during the last 3 months, reported by the patients/caregivers or assessed by the neurologist through the patient history. The patient must have seizures during the day to record them, not just seizures at night. ▪ Patients included in ICD-10 and ICD-10-GM classification as G40 with electroclinical manifestation of seizures. o G40.1 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple focal seizures o G40.2 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex focal seizures o G40.3 Generalized idiopathic epilepsy and epileptic syndromes o G40.6 Grand mal seizures, unspecified (with or without petit mal). According to medical criteria and electroclinical seizure manifestations (focal, focal-generalized or generalized onset seizure with a normal interictal EEG recording). o G40.8 Other epilepsies (Epilepsies and epileptic syndromes, undetermined whether focal or generalized). According to medical criteria and electroclinical seizure manifestations (focal, focal-generalized or generalized onset seizure with a normal interictal EEG recording). ▪ In case of epileptic syndromes not listed in the above or shows some of the syndromes mentioned in the

exclusion criteria, patients could be included according to medical criteria defined by the clinician. These criteria must be accordingly justified by the clinician (e.g., focal or generalized onset seizures without encephalopathy and with a normal interictal EEG recording). ▪ Ability to navigate in Android or iOS operating system. If mild or moderate disability, family members can assist with navigation if patient is unable. The smartphone must stay with the patient to record EEG, but seizures are registered by a family member
Exclusion criteria
▪ Presence of psychogenic seizures. o If there is a coexistence of epileptic and non-epileptic seizures, it will be considered an exclusion criterion if the patient or family cannot differentiate between the two types of seizures. o If the patient or family can always differentiate between the two types of seizures, the patient could be included in the study according to medical criteria (but only recording the epileptic seizures.) ▪ Psychiatric, neurological, or systemic disorders that the researcher believes could affect the realisation and interpretation of the results. ▪ Presence of more than 10 seizures per day on a habitual basis. ▪ Presence of epilepsia partialis continua (G40.5) ▪ Patients with legal representative ▪ Pregnant women ▪ Patients with only absence seizures (G40.A,G40.4) ▪ Patients with only myoclonic seizures or epileptic spasms (G40.B,G40.4). ▪ Patients included in ICD-10 and ICD-10-GM classification and not included in the medical criteria for specific epileptic syndromes in inclusion criteria. o G40.0 Localization-related (focal)(partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset o G40.4 Other generalized epilepsy and epileptic syndromes. In case of specific epileptic syndromes, patients could be included according to medical criteria (e.g., focal or generalized onset seizures without encephalopathy and with a normal interictal EEG recording) o G40.5 Epileptic seizures due to external causes*[4] or Special epileptic syndromes*[5] o G40.7 Petit mal, unspecified, without grand mal seizures o G40.9 Epilepsy, unspecified ▪ Participants in previous clinical trials with mjn-SERAS device. ▪ In the case the patient presents an epileptic syndrome mentioned in the exclusion criteria, the patient if the clinician considers the subject meets medical criteria to be included, the patient can be enrolled in the study. These criteria must be accordingly justified by the clinician (e.g., focal or generalized onset seizures without encephalopathy and with a normal interictal EEG recording

Table 2. Pilot study variables

Sociodemographic variables
1. Age 2. Sex
Background variables
1. Family History 2. Personal History: a) Pathologies during pregnancy b) Dystocia during childbirth c) Foetal distress d) Alterations in psychomotor development e) Difficulties in school performance f) Febrile seizures in childhood g) Cranioencephalic traumas h) CNS infections i) Psychiatric and/or neurological co-morbidities.
Epilepsy Variables
1. Current diagnosis: a) Main b) Secondary 2. Current pharmacological treatment, specification of the different AEDs 3. Alterations in cranial MRI 4. Alterations in blood tests 5. Alterations in CSF

6. EEG alterations
7. Alterations in physical or neuropsychological examination
8. Genetic test
9. Characteristics of seizures:
   a) Specific precipitants
   b) Accompanying signs
   c) Frequency of seizures
10. Types of seizures: According to the International League of Epilepsy (ILAE) classification
11. Refractory epilepsy
12. Baseline EEG with sleep deprivation
13. Quality of life index with QOLIE-31, QOLIE-AD-48 and EQ-5D-5L questionnaires, validated in Spanish, German and English version, at baseline and final period.
14. Number of accidents caused by seizures episodes
15. Emotional well-being with HADS and SCL-90-R questionnaire, for anxiety, depression and hostility, validated in Spanish, German and English version, at baseline and final period.
16. Physical functioning and role limitations due to physical health with PAM-13 questionnaires, validated in Spanish, German and English version, at baseline and final period.
17. Use of healthcare resources, frequency of use of resources.
18. Satisfaction with the ergonomic characteristics of the device, as well as possible adverse effects, mild or severe.

Mathematical Variables:

1. Energy features: average band energy, sum of bands, energy ratios, calculation of logarithms of energies and ratios.
2. Signal complexity measures: different entropies, mutual information, fractal dimensions and other calculations such as Hurst and Kolmogorov exponents.
3. Centrality measures: mean and median values, kurtosis and skewness of frequency and spectral distribution, frequencies, standard deviation, variance and spectral calculations.
4. Connectivity measures: cross-ratios, spectral and imaginary coherence, and weighted phase shift.

mjn-SERAS Device

The mjn-SERAS device is a portable device similar to a hearing aid that detects the brain electrical activity using three sensors (Figure 1), allowing the analysis of the data collected with a complex mathematical algorithm that is subsequently able to determine the possibility of presenting epileptic seizures, issuing an alert to the user at least one minute before the seizure that allows the user to take safety measures in case of such an event. The device has the CE mark under MDR for Europe, by notified body BSI Group, CE 777314.

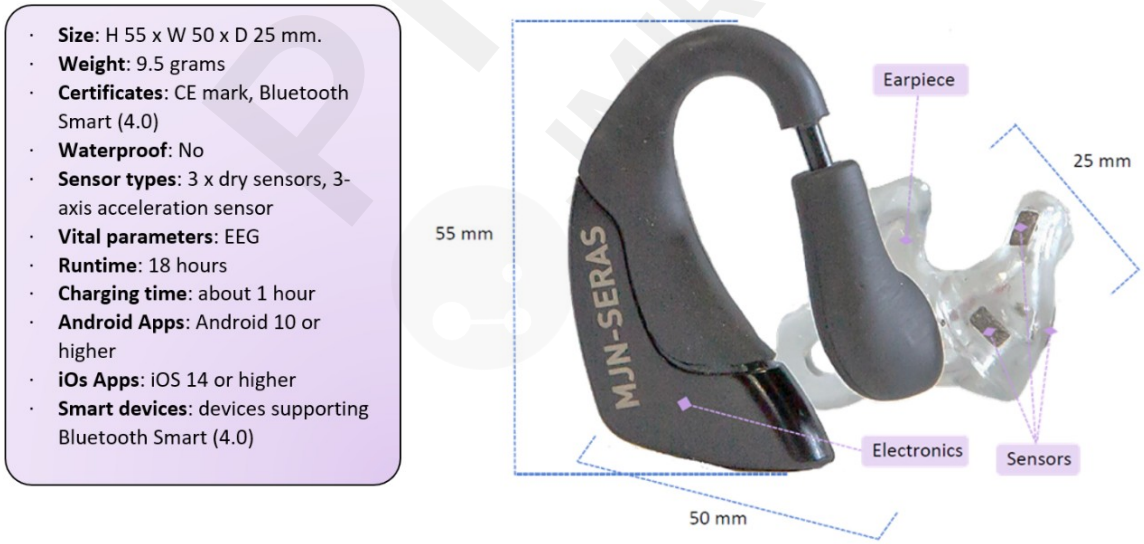

Figure 1. Specifications for the device

Seizure validation

All epileptic seizures reported by the patient will be recorded in the mobile application and will be stored in the server with all recorded data. It will then involve a double check process for validating the seizures, one from an automatic software and another

with an EEG human review. The first step involves an automatic software to detect the activity of the seizures in the EEG, checking that there is an electrical discharge, according to the criteria from all other seizures recorded. This software will work on the cloud server and will process all seizures reported by patient, validating those that are really seizures. The second step, the human review, will be the review of all seizures marked by the patient in the application and those detected by the artificial intelligence software by a neurophysiologist or neurologist specialised in epilepsy and EEG. The physician will review the recorded EEG with graph elements as used in routine video-EEG practice.

As has been pointed out in this project, the information processing applied will be based on a methodology centred on Artificial Intelligence and customisation of algorithms with the capacity to generalise alerts of possible seizures within a time window. To this end, it is extremely important and even critical to obtain a database that meets a series of requirements: to be sufficiently broad and representative, to contain relevant information on the time that the alert takes place on the device, onset of the seizure according to the clinical criteria of the patient and/or family/caregiver, relationship with the activity they were performing at the time, and reaction of the patient upon learning of the alert. All participants and their families will be informed that the device is in the clinical study phase, so that none of the alerts generated can be considered to be in "real mode", as this could have important consequences on the credibility of data not yet contrasted.

The participant must wear the device for at least 60 days at a rate of 10 hours a day (except when sleeping) and without altering their normal life activity as a result. The participant will have a contact telephone number that will be answered 12 hours a day during the participation in this study, allowing to answer any queries or deal with any incidents that may arise.

Screening and Recruitment

All the participants are voluntarily invited to the study and then required to sign an informed consent form containing information on the regulatory authorities and the related procedures, Recruitment of the participants would be based on inclusion criteria. The hospital must maintain a log register that records all the details of the screened participants and the reasons for exclusion. After recruitment the participants would be randomized and allocated to the intervention or the control group. The allocation to the intervention or control group takes place after the inclusion visit in the respective study centre via a tool called Research Randomizer. (https://www.randomizer.org/). To prevent bias, randomization will only occur after the inclusion visit is complete.

Follow-up of participants

During the period that the participant wears the mjn-SERAS device, the following follow-up will take place to verify the correct functioning of the device, as well as possible incidents that the participants may report (Table 3). The clinical personnel participating in the postmarked study are therefore recommended to perform a check-up 7, 15 and 30 days after implantation of the SERAS device, with subsequent check-ups every 30 days, to assess general operation, comfort and any aspects that the participants consider appropriate or generate doubts to them.

A face-to-face or online visit will also be proposed every 60 days with a research neurologist to analyse the seizures presented during the study period and check the records made by the mjn-SERAS device with the engineers, as well as to deal with the different observations and/or or suggestions made by patients. A final face-to-face interview will be held at the end of the postmarked study period with the neurologist and a neuropsychologist from the research team to close the participation in the postmarked study, collect the equipment and verify the last recordings made, assess the satisfaction in participating in the postmarked study and collect possible suggestions and points for improvement provided by the participants.

The team of psychologists and neuropsychologists of the project will perform an individualised interview at the beginning and at the end of the participant's study period to perform different scales and questionnaires with the aim of assessing the baseline and final state based on the social and mental well-being of the participants being studied. The usual activities, treatment and follow-up of the patients will not subject to participation in the study, who will follow strictly medical criteria in accordance with their usual practice, and no decisions will be made on treatment or follow-up based on the results obtained by the device in each participant. The data from the evaluation of the mjn-SERAS device, both during the registry and in the evaluation of the possibility of seizures taking place derived from the analysis and processing of the MJN algorithm, as well as the data resulting from the different surveys and questionnaires to analyse social and mental well-being changes, will be included in an SPSS database. These data will be analysed and cross-checked with other clinical characteristic variables on semiology, lateralisation, type of epilepsy, aetiology and sociodemographic variables.

Table 3. Clinical study visits calendar

Visits Procedure	Pres. V0	Telem. V1	Telem. V2	Telem. V3	Telem. V4	Telem. V5	Telem. V6	Telem. V7	Pres. V8
Inclusion/Exclusion criteria	X								
Informed consent signature	X								
Neurologic evaluation	X								
Seizure type description	X								

Evaluation visit		X			X		X		X
Clinical study data	X								X
Technical system data			X						
Technical system data and seizures				X		X		X	

Sample size and statistical considerations

This study is a clinical postmarked study that will serve as a basis and validation of the mjn-SERAS device as an early detection system for epileptic seizures. It is therefore necessary to start from a database with clinical information that allows processing of the basic information to develop an initial statistical interpretation and reach conclusions that allow us to assess the usefulness of the device according to the aforementioned functionality. Each patient is estimated to have a minimum of 12 seizures per record during their participation in the trial, and it is expected to obtain a sensitivity, specificity and F-Score greater than 70%, and an accuracy value greater than 70%, in the correlation of the mjn-SERAS device with the patient or relative's own detection, as well as in the generation of alarms after evaluating the possibility of presenting a crisis by the MJN algorithm. Given the lack of previous data, it is estimated that we will include 150 patients in this study with the criteria and variables of the project, which will allow us to have certainty in the results obtained and may be increased later if deemed appropriate in the future.

All statistical tests will be carried out at the 5% (two-sided) significance level unless otherwise specified. Estimates along with 95% confidence intervals and associated p values will be reported. The significance level will be estimated at $p<0.05$. Prevention is far superior to a statistical cure, and every effort will be made to collect outcome data on all participants. Missing values represent a potential source of bias in a clinical trial. Hence, every effort should be undertaken to fulfil all the requirements of the protocol concerning the collection and management of data. For example, we will ask medical staff at the clinical practices to obtain data on individuals who have stopped participating in the trial. The underlying missing data process determines the biasing effects of missing data and structures valid analytic strategies. If data are missing completely at random, then there is no induced bias and a complete case analysis, while inefficient, is valid. Another approach to dealing with missing data is assuming than on missing data we will use the last one used.

In terms of device performance, we have automated all data collection, so we only need to have the device working and connected to internet in some days, this is a simple way to provide as much data as possible in the clinical trial. Confirmations of seizures or other activities will be performed by the mobile application, so we can make a reminder each time that a data is loss. All statistical analyses will be performed using SPSS version 23 - STATA 14 software, from IBM SPSS Statistics.

Confidentiality and processing of personal data

In accordance with the provisions of Regulation (EU) 2016/679, dated 27 April, regarding the protection of natural persons with regard to the processing of personal data and with Organic Law 3/2018, on Data Protection and guarantee of the digital rights, the processing of the data related to the EEG will be exclusively limited to the development of activities related to the development of this Study. Both the participating centres and MJN, the latter in its capacity as Sponsor, are respectively responsible for processing the data contained in their information systems and will assume the commitment to comply with the aforementioned current regulations on data protection.

Data statement

The data collected for this study will be subjected to a prior process of pseudonymisation by the referring centre assigning it a unique and identifiable code only by the aforementioned Sponsor through an information encryption algorithm, and that cannot be identified by personnel outside the main research team. It will therefore no longer be possible to establish the link between the clinical care and electroencephalographic data to be analysed and the identity of the participating subject to which it refers by any reasonable means. Thus, data will not be included to identify the holders of the electroencephalographic records on which the study is performed, where only the authorised personnel of the participating sites and the Sponsor will be able to relate said data with the identity of the patients to whom they belong. Therefore, the identity of the participants will be absolutely confidential and will not be revealed to any other person, agent or entity, except when required by the health authorities or in cases of medical emergency. MJN, in its capacity as Sponsor, and despite pseudonymising the information on which the study documented here is to be performed, does not plan to carry out any international transfer of data to any country outside the community area, except for aggregate information or results, which, is not planned or protocolised on the current date of this Protocol. The confidentiality of the information is guaranteed, so that no person can be recognised through the presentation of results, as well as compliance with the requirements of the Declaration of Helsinki and Royal Decree 1090/2015.

Ethics approval

This study will be subject to prior authorisation from an accredited Medicines Research Ethics Committee (CEIm), more specifically, the Regional Ethics Committee for Drug Research of the Community of Madrid in Spain, Ref.:57/372589.9/22; Wales Research Ethics Committee 4, Wrexham for Oxford in UK, IRAS 323204, REC Reference : 23/WA/0196 ; Ethik-Kommission Universität Freiburg for Kork in Germany. EK-Frieburg Nr : 23-1531.

The time that the data subject to analysis must be stored will be limited to the legal terms established for that purpose by the regulations on data protection and clinical research. Subsequently, said information will be stored in a locked format without the possibility of any further processing, unless it is reused in the terms and conditions permitted by the applicable ethical criteria, by the applicable legislation on research with clinical documentation (including Law 41/ 2002, dated 14 November, Basic Law regulating the autonomy of the patient and the rights and obligations in terms of information and clinical documentation) and by the regulations on the protection of personal data (among others, Organic Law 3/ 2018, on Data Protection and Guarantee of Digital Rights).

This is a non-invasive interventional study, with minimal potential risk for the patient, in which the procedure to be followed to evaluate and validate the operation of the device will be explained in detail. It is a non-invasive electronic device the purpose of which is the evaluation of the likelihood of epileptic seizures taking place. This study will also include the contracting of civil liability insurance under the terms and conditions required by Royal Decree 1090/2015.

The group of researchers is led by Dr. Antonio Gil-Nagel as Research Director of the Department of Neurosciences at Clínica Corachan, accompanied by a relatively young team who are still deeply connected with other research groups, both national and international through different working groups from Spanish and European Scientific Societies. All this guarantees the rapid dissemination of this knowledge and opens the door to future collaborations in projects financed by public bodies as well as collaborative projects with private entities or technological developers.

RESULTS

This study is funded in 2022 by the EIT Health and European Union, under the programme EIT Health Amplifier n. 220445-230126. As of February 2025, we enrolled 76 patients in 6 clinical sites in Spain, UK and Germany. Data analysis is currently underway, and the first results are expected for June 2025.

DISCUSSIONS

Expected findings

Epilepsy is a chronic disease with approximately one third of patients resistant to anti-seizure medication (ASM). Outpatient follow-up is subjective according to the patient's account and the treating physician's interpretation of the information received. However, there are currently no mobile devices that allow early detection of seizures, the evolution of the disease, the severity of seizures, their frequency or duration. Hypothesized that the use of an intra-aural EEG device (mjn-Seras) will allow the recording of electroencephalographic activity and the subsequent processing of the data by the artificial intelligence algorithm of MJN to anticipate the event of suffering an epileptic seizure in those patients already diagnosed previously; and consequently, generate alerts prior to the onset of clinical symptomatology that allow the patient to take appropriate safety and prevention measures, and even alert of the possible future situation.

It is possible that the participants will not obtain a direct benefit from their participation. However, the validation or improvement of this device, whose objective is to generate alarms warning of epileptic seizures, may benefit in the future the participants themselves as well as other patients suffering from this disease and contribute to a better understanding and treatment of this disease.

There has been no other device like the mjn-SERAS on the market up until now or in previous phases of research, which has been able to consistently demonstrate the operation of a system for generating alerts about the possibility of having seizures or a mathematical algorithm that allows the analysis, assessment and identification of early signs in the detection of this type of seizure. A system that allows the analysis of the EEG data collected by the device to initially perform a learning process and subsequently generate an assessment of the likelihood of having a seizure would represent an important innovation in improving the quality of life of people with epilepsy, and an important advance in the knowledge and control of the pathology by medical professionals.

This study proposes the use of the mjn-SERAS device during the day-to-day life of the patient to analyse its performance in

generating alerts in the case of the possibility of a high risk of epileptic seizures and to evaluate the concordance and prediction of the generation of early detection seizure alarms, prior to the identification of these clinically manifested events and collected by the patient or their relatives.

In addition to the evaluation of these preventive alerts that we can associate with the physical sphere of the concept of health, we are going to determine, study and analyse the impact of the mjn-SERAS device on psychic and/or mental well-being as well as its repercussion on the social well-being of people with refractory epilepsy.

Study strengths and limitations

SERAS-Home is the first study investigating the use of seizure prediction algorithms in a normalised environment for the patient. It is a multi-centre study with 3 different countries and 6 hospitals, with a controlled and randomised design.
Patients' monitoring is developed through automatized algorithms, resulting in more control about the use of the device and less disconnections from the patients.
Totally anonymized data from the patients is generated from each device, so patient relationships is only available with hospital data or patient request.
Follow-up of the study participants is planned for 6 months, for better understanding of the quality of life improvement, we cannot calculate the loss to follow-up, which might reduce the sample size.
Study participants is limited to already diagnosed patients from the different hospitals.

Authors contributions

The study concept and design were conceived by AT and DB. AT wrote the first draft of the protocol, and all other co-authors reviewed it and contributed to the final version. All authors agreed on the final version executing it.

Funding statement

This work was supported by EIT Health and European Union, grant number 220445-230126.

Competing interests

None declared

The period of conservation of the data under analysis will be limited to the legal periods established for this purpose by the regulations on data protection and clinical research.

Keywords

Epilepsy; medical device; early detection; seizure prediction; artificial intelligence;

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Supplementary Files

Figures

Device specifications.

- **Size**: H 55 x W 50 x D 25 mm.
- **Weight**: 9.5 grams
- **Certificates**: CE mark, Bluetooth Smart (4.0)
- **Waterproof**: No
- **Sensor types**: 3 x dry sensors, 3-axis acceleration sensor
- **Vital parameters**: EEG
- **Runtime**: 18 hours
- **Charging time**: about 1 hour
- **Android Apps**: Android 10 or higher
- **iOs Apps**: iOS 14 or higher
- **Smart devices**: devices supporting Bluetooth Smart (4.0)