NICE advice

24/7 EEG SubQ for epilepsy

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is 24/7 EEG SubQ. It is a subcutaneous electroencephalogram (EEG) recording device for people with epilepsy. The system consists of an EEG electrode designed for subcutaneous implantation, an external recording device and data reduction software EpiSight.
- The **innovative aspects** are that it offers ultra-long-term monitoring (30 days and over) for people with epilepsy in their day-to-day life.
- The intended **place in therapy** would be in addition to standard care as an option for long-term monitoring to help manage epilepsy.
- The **main points from the evidence** summarised in this briefing are from 5 studies, including 2 case studies and 3 case series with a total of 11 adults. They show that the 24/7 EEG SubQ identifies additional seizure counts and seizure pattern information to inform individual management plans.
- **Key uncertainties** around the evidence are that the evidence base is small and of low methodological quality, with small sample sizes and a high risk of selection bias.

- **Experts advised** that the system could improve epilepsy management for a small subgroup of people. But, there needs to be consideration of the value on a case-by-case basis with understanding of the probable location of the seizures for the correct placement of the system to capture them.
- The **cost** of 24/7 EEG SubQ system is about £13,500 (excluding VAT), including the subcutaneous implant, external device and software. Additional costs include anaesthetic, anaesthetist and surgeon costs. The resource impact would be in addition to standard care when seizures remain uncontrolled and true seizure burden is not well understood.

The technology

The 24/7 EEG SubQ device (UNEEG Medical) is an electroencephalogram (EEG) recording device for people with epilepsy. The system is intended to monitor seizures for adults with uncontrolled epilepsy, when treatment has been adjusted and seizures remain uncontrolled or when there is a doubt about the true seizure burden being experienced. As a monitoring tool, it is intended to capture an objective count of frequency, type and circadian distribution of seizures. The implant can stay in place for up to 15 months to help identify seizures happening during daily life over a long time period.

The system consists of an EEG electrode designed for subcutaneous implantation, an external recording device and data reduction software EpiSight. The subcutaneous implant measures the EEG from 2 bipolar channels with a common reference. The device has a limited spatial coverage and lower spatial resolution than routine diagnostic EEG, which can routinely have between 12 and 64 channels. The systems software, EpiSight, has a front-end seizure detection algorithm that was developed in collaboration with the Austrian Institute of Technology (AIT). The software aims to provide continuous EEG biomarker information to support healthcare professionals in epilepsy management.

Innovations

The company reports that 24/7 EEGSubQ is the first CE-marked EEG recorder for ultra-long-term monitoring of epilepsy. The system aims to help identify and manage the true seizure burden for individuals with suspected epilepsy when routine EEG and patient diaries are inadequate. The device is unobtrusive and can be used outside of hospital for people in their day-to-day life.

Current care pathway

Current standard care recommends that all adults with a new onset suspected seizure should be seen urgently (within 2 weeks) by a specialist. The diagnosis of epilepsy involves detailed history taking with the individual and any family members. If the diagnosis cannot be clearly established, further investigations will be considered. An EEG should only be considered to support a diagnosis of epilepsy in adults in whom the clinical history suggests that the seizure is likely to be epileptic in origin. If a routine EEG does not provide sufficient information, further investigations should be considered, including a sleep-deprived EEG, ambulatory EEG or video telemetry (for more information about EEG, see the NHS website).

Clinicians assess the effectiveness of anti-seizure drug therapy based on patients' seizure diary at outpatient visits every few months. If seizures are not controlled or there is diagnostic uncertainty or the treatment does not work, individuals should be referred to tertiary services within 4 weeks for further assessment. In some instances, long-term video-EEG (video telemetry) may be considered, if it is expected a 5 to 10-day monitoring period could capture seizures. The test involves a planned hospital admission over the scheduled period (between 5 to 10 days) but is not available at all centres. People may continue to need therapy adjustments as part of their follow-up consultations to better manage their condition. Neuroimaging using MRI may be used to assist in the care pathway more often in adults when seizures continue with first-line medication.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on epilepsies: diagnosis and management
- NICE's guideline on suspected neurological conditions: recognition and referral
- NICE interventional procedures guidance on deep brain stimulation for refractory epilepsy in adults
- NICE interventional procedures guidance on vagus nerve stimulation for refractory epilepsy in children
- NICE interventional procedures guidance on MRI-guided laser interstitial thermal therapy for drug-resistant epilepsy
- Scottish Intercollegiate Guidelines Network (SIGN) guideline on epilepsies in children and young people: investigative procedures and management

Population, setting and intended user

Epilepsy is a common neurological disorder characterised by recurring seizures. It is difficult to accurately estimate incidence and prevalence because identification is challenging, but it has been estimated to affect between 362,000 and 415,000 people in England.

The 24/7 EEG SubQ system is intended for individuals when seizures are not well controlled or if treatment does not work. It aims to provide additional information on the seizure burden to inform seizure management. The system can be used in specialist outpatient clinics by trained healthcare professionals, which may include surgeons, neurologists, clinical physiologists and neurophysiologists. The device is available in 2 variants, including a magnet (M1) and an alternative clip attachment with no magnet (C1). Clinicians should consider if either system is appropriate according to the instructions for use in the 24/7 EEG SubQ user manual. Contraindications to the system include people with other active implants such as cochlear implants, people having therapies with medical devices that deliver energy around the area of the implant and people with a hobby or profession that includes extreme pressure or risk of trauma to the device site.

The selected implant should be inserted subcutaneously with a supplied needle under local anaesthesia by a surgeon trained with the device. The outpatient procedure should take 15 to 30 minutes. Full details can be found in the 24/7 EEG SubQ company user manual for surgeons. All people who have the implant should be issued with a medical implant ID card. After around 10 days, once the stiches have healed, the recording can then begin. The company reports that a high number of people use the device as intended, with reported average recordings of 18.5 hours per day.

Follow-up care may vary from clinic to clinic. But, it is recommended the recordings are reviewed by the neurologist, with support from the neurophysiology team, for consideration in the future management plan.

Costs

Technology costs

The cost of the full system is about £13,500, including the subcutaneous implant, external

device and software. Device implantation has additional costs including the local anaesthetic (costing between £5 and £23, BNF online), the anaesthetist and a trained surgeon.

Costs of standard care

Further testing may be requested. This includes long-term EEG (12 to 72 hours) at an average of £366 per test, or video telemetry EEG at a cost of around £2,000 per day (for a 5- to 10-day monitoring period). Additional costs because of uncontrolled seizures might include unplanned trips to the emergency department, costing around £133 per attendance. This may result in non-elective hospital admissions that can cost between £404.17 and £2,030.88 for short stays. Follow-up neurology consultations cost about £199 per attendance. Further costs may be accrued because of therapy modifications to manage ongoing uncontrolled seizures. (National schedule of NHS costs, 2018/19).

Resource consequences

The device is currently being trialled in a research capacity at a number of NHS trusts. Adopting the device would need increased resources including surgeons and anaesthetists for implantation under local anaesthetic in an outpatient setting. The company claims that while the device cost would be in addition to standard care, it could lead to greater benefits including better clinical management and improved patient outcomes. This could result in longer-term savings by reducing unplanned admissions.

A short introductory training for healthcare professionals is provided by the company at no cost. This is expected to take 60 minutes of clinician's time, with further quick guide resources provided to support implementation. The healthcare professional is supported by the company on request for the first user. It is suggested that a surgeon do a minimum of 3 implantations before considering training other surgeons themselves in the procedure.

Regulatory information

The 24/7 EEG SubQ is a CE-marked class III medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

People from a socioeconomically deprived background are at higher risk of developing epilepsy. Incidence studies show that epilepsy may be more common in men than women, but this varies across types of epilepsy and is rarely a significant difference. Incidence of epilepsy is at its lowest between the ages of 20 and 40 and steadily increases after age 50, with the greatest increase seen in those over age 80. People with a learning difficulty have higher rates of epilepsy than the general population; making up about 25% of the total of people with epilepsy and 60% of people with treatment-resistant epilepsy (Royal College of Psychiatrists report on prescribing antiepileptic drugs for people with epilepsy and intellectual disability, 2017). Some people with epilepsy may be covered by the Equality Act 2010 if their condition has had a substantial adverse effect on normal day-to-day activities for over 12 months, or is likely to do so.

The device is contraindicated for use alongside other active implants such as cochlear implants. Some individuals with implants such as cochlear implants may be considered disabled. It is also contraindicated for use alongside therapy that delivers energy using medical devices around the site of the 24/7 EEG SubQ implant. Some individuals having these therapies may be considered disabled. The system needs user operation, so user selection must consider if the person can operate the device independently. If not, whether there is an appropriate caregiver who can help operate the system on their behalf. This may include people with mental health problems, cognitive impairments or physical impairments. These individuals may be considered disabled and disability is a protected characteristic under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

Five studies are summarised in this briefing. The evidence comes from descriptive feasibility studies, including 2 case studies and 3 case series involving a total of 11 adults. Two case series (Weisdorf et al. 2018, Gangstad et al. 2019) reported on are early subpopulations of Weisdorf 2019.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The published evidence suggests that the 24/7 EEG SubQ can identify additional seizure counts and seizure pattern information compared with standard care, to inform individual management plans. The evidence base is very limited, of low methodological quality, with a high risk of selection bias and small sample sizes.

Viana et al. (2020)

Study size, design and location

Case report of a 35-year-old woman with refractory epilepsy (n=1).

Intervention and comparator

24/7 EEG SubQ and patient diary.

Key outcomes

The study found that there was substantial agreement between days of reported and recorded seizures, although multiple clustered seizures remained undocumented. Circular statistics identified significant subcutaneous electroencephalogram (EEG) seizure cycles at circadian (24-hour) and multidien (5-day) timescales. No adverse events were reported.

Strengths and limitations

A case report limits generalisability. There is the potential for missed seizures because of

limited spatial sampling of the device. One author is an employee of UNEEG medical and another had worked with the company on an unrelated research study.

Weisdorf et al. (2020)

Study size, design and location

Case report of a 42-year-old woman with temporal lobe epilepsy (n=1).

Intervention and comparator

24/7 EEGSubQ.

Key outcomes

The study found that the subcutaneous EEG device was used for 76 days (with 63% usage) and revealed unrecognised breakthrough seizures. These results informed treatment response, prompting treatment adjustment. No adverse events were reported.

Strengths and limitations

The device has limited spatial coverage of brain areas, which may not capture all seizure events. No conflicts of interest were reported.

Weisdorf et al. (2019)

Study size, design and location

Case series of 9 people at Zealand University, Denmark.

Intervention and comparator

24/7 EEG SubQ.

Key outcomes

Case series of 9 people who had the subcutaneous EEG monitor implanted. Recording of

490 days of EEG was collected across 8 people completing at least 9 weeks of home monitoring. One person did not continue. The study found that the device revealed unrecognised seizures and informed treatment adjustment. Five participants appeared to have circadian rhythms and 2 individuals had too few seizures to establish a trustworthy pattern. No serious adverse events were reported. Most participants experienced soreness on the implantation site after the surgery, this passed within a week for 6 people and 2 people had longer lasting soreness for 2 and 4 weeks, respectively. Two individuals reported occasional headaches during the study. For one this was mild and for the other this was moderate and needed over-the-counter pharmacological treatment (this person had similar occasional headaches before to the study). One unclassified event was described as a tingling sensation in the implant, only while in specific locations at home. Technical examination of the implant after explanation revealed no malfunction. User experience information was collected anecdotally with people taking part in the study, who reported that the device was easy to use. Some minor annoyances were reported, but people reported that they did not feel constrained in their ability to do jobs or leisure activities.

Strengths and limitations

Two authors are fulltime employees at UNEEG. One has received support from the company, and another has previously performed consultancy for the company.

Weisdorf et al. (2018)

Study size, design and location

Case series of 4 adults at Zealand University, Denmark.

Intervention and comparator

EEGSubQ and long-term video scalp EEG.

Key outcomes

All recorded seizures were classified as temporal lobe seizures and there was 100% lateralisation match. One person reported slight soreness around the site, that receded gradually during the admission. For 1-person large parts of the subcutaneous EEG recorded during wakefulness was contaminated by high-frequency muscle artefacts,

which almost completely disappeared during sleep. The study reported high similarity between subcutaneous EEG channels and nearby temporal scalp channels for most EEG events. The study concluded that subcutaneous EEG recordings are very similar to scalp recordings in both time and time-frequency domains, if the distance between them is small.

Strengths and limitations

The authors acknowledge the limitations of the data and present it as preliminary results contributing to a growing mass of evidence. The authors suggest that as many electroencephalographic events are local or regional, the positioning of the subcutaneous electrodes should be considered carefully to reflect the relevant clinical question. The effect of implantation depth of the subcutaneous electrode on recording quality should be further investigated. Two authors are full-time employees of UNEEG Medical and one further author has consulted for the company.

Gangstad et al. (2019)

Study size, design and location

Case series of 4 adults at Zealand University Hospital, Denmark.

Intervention and comparator

24/7 EEGSubQ and long-term video scalp EEG.

Key outcomes

Shows effective automatic sleep score for people with 2 channel subcutaneous EEG, which are comparable to in-clinic recordings. An average Cohens kappa of k=0.78 (plus or minus 0.02) was achieved using patient-specific leave-one-night-out cross validation. When merging all sleep stages into a single class they reported to have 94.8% sensitivity and 96.6% specificity. Compared with manually labelled video-EEG, the model underestimated total sleep time and sleep efficiency by 8.6 minutes and 1.8 minutes, respectively. It overestimated wakefulness after sleep onset by 13.6 minutes. No adverse events were reported.

Strengths and limitations

Recordings were done in hospital with healthcare professional monitoring. The patient cohort is the same population reported in Weisdorf et al. 2018 and the subpopulation of Weisdorf et al. 2019. Three authors are UNEEG medical employees and a further 2 authors are partially funded by UNEEG medical.

Sustainability

The company did not report any sustainability benefits of the technology.

Recent and ongoing studies

- Ultra-long-term sleep monitoring using UNEEG medical 24/7 EEG SubQ. ClinicalTrials.gov identifier: NCT04513743. Status: active. Indication: epilepsy. Devices: 24/7 EEGSubQ system. Date: April 2021. Country: Denmark.
- Evaluation of the 24/7 EEG SubQ system for ultra-long-term recording of patients with temporal lobe epilepsy an open-label, prospective, paired, comparative study. ClinicalTrials.gov identifier: NCT04526418. Status: recruiting. Indication: epilepsy. Devices: 24/7 EEG SubQ system. Date: August 2023. Country: the US and Germany.
- Subcutaneous EEG: forecasting of epileptic seizures (SUBER) an observational, non-randomised, non-interventional study. ClinicalTrials.gov Identifier: NCT04061707. Status: recruiting. Indication: epilepsy. Devices: 24/7 EEG SubQ. Date: May 2022. Country: UK.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

One individual has done research with this technology and 3 experts had not used the technology.

Level of innovation

Two experts identified the system as novel and of uncertain safety and efficacy. Another agreed that it was a major change to the standard method but that it was one of a few implantable devices currently available. Another expert felt it was an interesting development of an existing procedure.

All experts agreed that this device would not replace standard care but could be used for a small subgroup population alongside standard care. One expert identified a number of opportunities the device could offer. These included monitoring in the community, long-term monitoring allowing observation of patterns in seizures to be identified, including considering treatment response.

Potential patient impact

Two experts reported the main benefit to be more accurate monitoring of seizure frequency and burden than is currently possible with a diary-based system. One expert highlighted that this feedback is critical for management decisions, treatment choices and the effect of lifestyle changes.

Experts reported that the device may have potential in a small group of patients in a diagnostic grey area. This includes those who have frequent seizures when it may help monitor the efficacy of treatment more quickly or help the diagnosis in those who are unable to accurately document the number of seizures they are having. One expert said they felt that individuals with drug-resistant epilepsy and people participating in drug trials may also benefit from this device. One expert felt that it could help find optimum medication regimens more swiftly, potentially leading to fewer outpatient clinic appointments and unscheduled visits. Two experts highlighted that the limited spatial coverage means there is a risk of missing true focal seizures, highlighting the importance of using previous knowledge about the seizure focus to inform the best area to place the implant.

Potential system impact

Experts felt that the system is unlikely to change the current pathway in its present form. One expert highlighted that although the high sensitivity may mean more accurate reporting, people will still need a review because it does not replace the need for in-

person reviews of pharmacological changes.

All experts described the adoption of this system to be more expensive than standard care because of the high cost of the device alongside the ongoing cost of standard care. One expert highlighted that this may be offset by reduced outpatient, diagnostic and unscheduled care costs that need to be considered.

All experts raised the need for training, including for implantation and the acquisition and review of acquired data. Two experts said the facilities and time to accommodate the surgical procedure would be more than standard surface electrode placement setting needs, alongside increased time and resources.

Experts highlighted the changes to infrastructure that would be needed to allow clinicians to access the output of the device with relevant IT infrastructure. One expert queried the storage process and whether the data would benefit from being centralised to provide sufficient expertise, if required this would mean patients using these systems may need to attend tertiary centres.

General comments

Experts highlighted some considerations around side effects with the implant, with 2 experts highlighting the pain reported in 2 of the summarised studies. Both studies provided further details that the soreness reported had passed within the study period. Two experts queried the risk of infection with subcutaneous implants, which is a listed possible side effect in the instructions for use (no instances of this are reported in the evidence base).

While the system offers long-term monitoring, 3 experts highlighted the limited spatial sampling the system has as a result. One expert advised that clinicians would need to be satisfied there was a significant chance of relevant seizures being captured before implantation. Two experts highlighted the reported artefacts in the studies that may cause false positives to be recorded. One expert added that using an invasive monitor (albeit minimally invasive), is contentious when the clinical impact of the events being detected is uncertain, highlighting again the importance of patient selection.

Patient organisation comments

Key benefits for patients identified by patient organisations included the ability to record seizures in the natural environment, without the need to be admitted to hospital. This can capture long-term data, increasing the likelihood of recording a seizure and potentially helping identify patterns of when seizures happen. One organisation highlighted that the device could improve understanding of the correlation between subjective reports and actual seizures, moving towards improved clinical management. One organisation reported that the device is understood to be well accepted.

Patient organisations noted that those who could particularly benefit from the system were those who remain in education, to reduce disruption through their care. Also, those who have limited access to healthcare through location and transport as subsequent appointment burden is reduced. One organisation advised that those individuals whose seizures vary would particularly benefit. Another organisation highlighted that people who find keeping accurate seizure diaries a challenge could particularly benefit from the technology. This may include individuals with memory difficulties or a learning disability.

Both organisations reported possible challenges of the technology, including that it may be more painful with increased side effects, including risk of infection. One organisation advised that it may not suit people who appreciate the engagement of regular clinician feedback. One organisation highlighted that the limited overlying cortical area being recorded may miss the 'area of interest', resulting in not providing sufficient data.

Organisations highlighted that some groups may need special consideration for this device. This includes individuals with challenging behaviour (autism or a learning difficulty), which may need significant parent or carer support to optimise device use for an extended time period with the intervention, particularly if they have head sensitivities. Older people and people with physical disabilities may have issues reattaching the device.

One organisation reported that neurophysiology does not currently have adequate automated algorithms for data analysis and they felt investment in artificial intelligence is needed in the long term to support the demand in the field.

Expert commentators

The following clinicians contributed to this briefing:

- Professor Ley Sander, professor and head of neurology, UCL Queen Square Institute of Neurology. Did not declare any interests.
- Ronit Pressler, consultant in clinical neurophysiology, Great Ormond Street Hospital for Children NHS Foundation Trust. Did not declare any interests.
- Rachel Thornton, consultant in clinical neurophysiology, Cambridge University Hospitals NHS Trust. Did not declare any interests.
- Rhys Thomas, honorary consultant in epilepsy, Newcastle University. Received financial support for a PhD fellowship as part of the Epilepsy Research UK Doctoral hub. Received payment for role in a symposium for the British Branch of the International League Against Epilepsy (ILAE).

Representatives from the following patient organisations contributed to this briefing:

- Epilepsy Action
- Young Epilepsy

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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