Automated real-time detection of tonic-clonic seizures using a wearable EMG device

Sándor Beniczky, MD, PhD, Isa Conradsen, PhD, Oliver Henning, MD, Martin Fabricius, MD, DMSc, and Peter Wolf, MD, DMSc

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Abstract

Objective
To determine the accuracy of automated detection of generalized tonic-clonic seizures (GTCS) using a wearable surface EMG device.

Methods
We prospectively tested the technical performance and diagnostic accuracy of real-time seizure detection using a wearable surface EMG device. The seizure detection algorithm and the cutoff values were prespecified. A total of 71 patients, referred to long-term video-EEG monitoring, on suspicion of GTCS, were recruited in 3 centers. Seizure detection was real-time and fully automated. The reference standard was the evaluation of video-EEG recordings by trained experts, who were blinded to data from the device. Reading the seizure logs from the device was done blinded to all other data.

Results
The mean recording time per patient was 53.18 hours. Total recording time was 3735.5 hours, and device deficiency time was 193 hours (4.9% of the total time the device was turned on). No adverse events occurred. The sensitivity of the wearable device was 93.8% (30 out of 32 GTCS were detected). Median seizure detection latency was 9 seconds (range −4 to 48 seconds). False alarm rate was 0.67/d.

Conclusions
The performance of the wearable EMG device fulfilled the requirements of patients: it detected GTCS with a sensitivity exceeding 90% and detection latency within 30 seconds.

Classification of evidence
This study provides Class II evidence that for people with a history of GTCS, a wearable EMG device accurately detects GTCS (sensitivity 93.8%, false alarm rate 0.67/d).

From the Department of Clinical Neurophysiology (S.B.), Danish Epilepsy Centre Dianalund and Aarhus University Hospital; FORCE Technology (I.C.), Hørsholm, Denmark; Department of Clinical Neurophysiology (O.H.), National Centre for Epilepsy, Oslo University Hospital, Norway; Department of Clinical Neurophysiology (M.F.), Copenhagen University Hospital Rigshospitalet; Department of Neurology (P.W.), Danish Epilepsy Centre, Dianalund, Denmark; and Postgraduate Programme in Clinical Medicine (P.W.), Federal University of Santa Catarina, Florianópolis, Brazil.

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Generalized tonic-clonic seizures (GTCS) may lead to injuries, and constitute the major risk factor for sudden unexpected death in epilepsy (SUDEP), especially in unattended patients.\(^1\)\(^2\) Wearable seizure detection devices were suggested to prevent SUDEP.\(^1\)\(^–\)\(^4\) The unpredictability of seizure occurrence is distressing for patients and caregivers.\(^3\) It contributes to social isolation and decreased quality of life, and surveys showed a need for wearable seizure detection devices.\(^5\)\(^–\)\(^10\)

Therapeutic decisions and clinical trials use self-reporting of seizures. However, this is unreliable: studies in video-EEG monitoring units demonstrated that 61% of seizures remain unrecognized by patients, even secondarily generalized tonic-clonic seizures, which remained completely unrecognized.\(^11\) Wearable devices could provide objective data about seizure occurrence.

Signals from muscles, recorded with surface EMG, seem to be a promising modality for detecting motor seizures. A recently published review summarizes the specific pathophysiologic changes in muscle activity during seizures.\(^12\) Quantitative EMG parameters differentiate epileptic from physiologic muscle activation and from nonepileptic seizures.\(^13\)\(^–\)\(^15\) Based on characteristic changes in frequency and amplitude, we have developed a generic seizure detection algorithm.\(^17\) High sensitivity and specificity of EMG-based seizure detection algorithms were found in 2 retrospective studies using offline analysis of EMG recorded with conventional amplifiers.\(^17\)\(^–\)\(^18\) A pilot study showed promising results for a wearable EMG-based device implementing our algorithm.\(^19\)

We present a prospective, multicenter study on the diagnostic accuracy of real-time detection of GTCS using the wearable EMG device. We report our findings according to the Standards for Reporting of Diagnostic Accuracy (STARD) criteria.\(^20\)

Inclusion criteria were (1) admission to noninvasive long-term video-EEG monitoring in the epilepsy monitoring unit (EMU) in one of the participating centers; and (2) historical data suggesting that the patient had GTCS. Exclusion criteria were (1) age under 3 years; (2) pregnancy; (3) allergy to the self-adhesive patch; or (4) implanted vagal nerve stimulator or deep brain stimulator.

Patients underwent video-EEG monitoring using wireless amplifiers (at the Danish Epilepsy Centre) or connected with a 10-meter-long cable (in the other centers). The mobility of the patients was not restricted in the EMUs, where patients were free to perform their habitual physical activities and participate in activities such as using an exercise bicycle, preparing coffee or food, and playing home video games involving body motion (Nintendo [Kyoto, Japan] Wii).\(^21\) Patients were under continuous surveillance and no injuries occurred during monitoring.

**Standard protocol approvals, registrations, and patient consent**

The project has been approved by the regional ethics committees (in Denmark: SJ-380; in Norway: 2013/2354). All patients (or guardians of patients) gave their written, informed consent prior to the study.

**Wearable EMG-based seizure detection device**

We tested the diagnostic accuracy of the Epileptic seizure Detector Developed by IctalCare (EDDI). The device measures surface EMG signals and was placed on the brachial biceps muscle (figure 1, A–D). The device is relatively small, and is easily hidden under the patient’s clothes. The choice of side for the placement was decided based on historical data where the patient’s seizures habitually were most strongly expressed. When there was no known side preponderance, the device was placed on the left.

The wearable device is attached to a self-adhesive hypoallergenic hydrogel patch (Axelgaard Manufacturing Co. Ltd., Fallbrook, CA) with 3 embedded surface EMG electrodes (bipolar recording electrodes and ground electrode), developed specifically for this device (figure 1C). The distance between the recording electrodes was 20 mm. A lithium polymer battery was placed into the wearable device.

Sampling frequency was 1,024 Hz. A modified version of the previously reported algorithm was implemented into the device.\(^17\)\(^–\)\(^19\) Briefly, the electrophysiologic biomarker of the initial phase of GTCS consists of an increase in amplitude and high-frequency (>150 Hz) oscillations in the EMG signal.
This was expressed as the number of zero-crossings, where high frequency oscillations (high-pass filtered at 150 Hz) exceeded a hysteresis of ±35 μV. The count of zero-crossings was calculated for a window of 1 second, with an overlap of 75% with the previous window. When this exceeded the predefined threshold, the alarm was triggered (figure 2). The measures are generic (not patient-specific), they were pre-specified before this study, and they were applied to all patients. The algorithm requires minimal computational power.

The device gives real-time seizure alarms and a different type of alarm for device deficiency, when electrode impedance is out of bounds. However, the study design implied blinding of the personnel for any data from the device, and therefore these alarms were disabled in this study. Instead, the device logged real-time all-seizure alarm time points, for comparison with the reference standard, and the periods with high impedance and 50-Hz artefacts were considered device deficiency periods. Detected seizure time points were read blinded to any other data. In addition, the EMG recorded by EDDI was transmitted via radio signals to a computer that stored the signals. The intention was to use these signals for further optimization and fine-tuning the measures of the algorithm. However, that is not reported in this study. All data presented in this study are based on real-time seizure detection using the predefined measures and the algorithm described above, with all calculations done on the wearable device.

The self-adhesive patch was changed once per day (standard procedure). The battery was changed 3 times per day; this is more than the standard procedure for the device, and it was necessary because in the study EMG data were transmitted to and saved on a computer. This increased significantly the power consumption of the device. For standard operation of EDDI (real-time computation, giving alarms and logging time points, without transmitting EMG data), change of the battery is required once per day.

Reference standard
The reference standard for identifying seizures was long-term video-EEG monitoring, reviewed by trained, board-certified clinical neurophysiologists and epileptologists, with more than 10 years’ experience with EMU (S.B., O.H., and M.F.). The experts were blinded to all data from EDDI, until they completed the analysis of the video-EEG recordings. For GTCS, they identified the start time point at the beginning of the tonic phase and the end time point at the end of the clonic phase. The time points of the reference standard were then compared with the logs of the real-time automated seizure

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Figure 1 Wearable seizure detection device (Epileptic seizure Detector Developed by IctalCare)

(A) The wearable device placed on the brachial biceps muscles. (B, C) The wearable device, which is connected to the self-adhesive patch, containing the recording electrodes and the ground electrode. (D) Remote control of the device.
detection. At the beginning of each monitoring, the times in
the device and in the video-EEG monitoring equipment were
synchronized.

**Study outcome measures**

The primary aim was determining the diagnostic accuracy of
the device. Sensitivity was expressed as the percentage of the
detected GTCS. Specificity was expressed as the false alarm
rate (FAR), calculated from the entire patient population.

In addition, we documented the following: adverse events
(any patient concern related to the device, reported by the
patient or observed by the personnel), device-off time (total
time when the device was turned off during monitoring—for
example, for changing patch and battery, time in bathroom,
ictal SPECT), device-deficiency time (periods with high
impedance and artefacts preventing the functioning of the de-
vice; this was expressed as percentage of the total time when
the device was turned on—i.e., the total recording time), and
detection latency (measured from the start time point iden-
tified by the experts to the alarm time point from the device).

**Classification of evidence**

The primary research question was the accuracy (sensitivity
and false-alarm rate) of a wearable EMG device for detecting
GTCS. This study provides Class II evidence that for people
with a history of GTCS, the wearable EMG device, EDDI,
detects GTCS with a sensitivity of 93.8% and a false-alarm rate
of 0.67/d.

**Sample size estimation**

For the expected sensitivity of 95%\(^\text{17,19}\) and expected preva-
lence of 28% in the studied population,\(^\text{22}\) with a confidence
interval (CI) of 10%, we needed 18 patients with GTCS and 65
recruited patients.\(^\text{23}\) GTCS is the seizure type with the highest
risk for the patients and therefore considered an undesired
event in EMUs.\(^\text{24}\) Diagnostic tapering of antiepileptic medica-
tion is aimed at increasing seizure frequency though avoiding
GTCS unless this is the targeted seizure type, and these occur
relatively rarely in EMUs. Our intention was to record GTCS
from 20 patients, with a total of at least 30 GTCS. Since the
quantitative EMG changes during GTCS have a high intra-
individual and interindividual consistency, this number seemed
to be sufficient to evaluate the performance of the device.\(^\text{14}\)

**Results**

The mean recording time per patient was 53.18 hours (me-
dian 53.12; range 2.3–130 hours). The device was turned on
for 3,928.6 hours. Device de-

diciency occurred in 193.1 hours
(4.9%). The total recording time was 3,735.5 hours. No ad-
verse events occurred.

Figure 3 shows the STARD flowchart of the study. Thirty-two
GTCS occurred during the recording time. Twenty of the 71
included patients had GTCS (11 patients had 1 seizure each;
6 patients had 2 seizures; 3 patients had 3 seizures).

The sensitivity of the device was 93.8% as it detected 30 out of
the 32 GTCS (95% CI 86%–100%). All GTCS were detected
in 18 patients (90% of all patients with GTCS). Two patients
with 2 seizures had only 1 seizure detected. Calculated per
patient, the mean sensitivity was 95% (median 100%; range
50%–100%). Four seizures from 3 patients with idiopathic
generalized epilepsy were primary GTCS; all of them were
detected. The other seizures were secondarily GTCS.

Both missed GTCS occurred as the second seizure after
a detected GTCS, with short interseizure periods (19 minutes
and 98 minutes, respectively). Retrospective inspection of
the EMG signals during the missed seizures showed low amplitude
of the EMG signal in one case, and very short tonic phase in the
other case, so that the number of zero-crossings did not exceed
the predefined detection threshold for any of the missed seizures.

The median detection latency of the device was 9 seconds
(range −4 to 48 seconds; mean 12.3 seconds), measured from
the start of the tonic phase of the seizures.
The false discovery rate was 0.02/h (i.e., 0.67/d). Two-thirds of the patients (47/71 [66%]) did not have false alarms. In 3 patients, the number of false alarms was ≥10. The most common reason for false alarms was physiologic muscle activation: physical exercise (68% of false alarms). The second most common reason was device malfunction: induction artifacts (18%) and detaching electrodes (2.5%). The vast majority of false alarms occurred during daytime. Only 2 nocturnal false alarms occurred: one was triggered by an episode classified as paroxysmal arousal, and the other one was triggered by stretching the arms during an arousal.

The ratio between false alarms and true alarms was ≤1 for 17 of the 20 patients with GTCS (85%), and in 13 patients with GTCS (65%) the ratio was zero (i.e., no false alarms recorded). The range of the ratio was between 0 and 14 (median 0; mean 1.3). A total of 161 seizures other than GTCS occurred during the recording: 59 simple partial seizures (11 patients), 55 complex partial seizures (14 patients), 26 myoclonic jerks (5 patients), 6 absences (2 patients), 1 nonconvulsive status epilepticus, 14 convulsive psychogenic nonepileptic seizures (5 patients). None of these triggered seizure alarms.

**Discussion**

In this prospective, multicenter, blinded study on the accuracy of real-time detection of GTCS using an EMG-based wearable device (EDDI), we found that it had high sensitivity (93.8%) and short detection latency (9 seconds). Specificity of the device was reflected by the low number of false alarms (0.67/d). None of 161 seizures other than GTCS triggered an alarm.

As the study was blinded, the alarm function of the device was turned off in this study. Nevertheless, the short detection latency suggests that timely warning is possible using this device. Large field studies, with long-term, ambulatory use of the device, are necessary to evaluate its potential in reducing the number of seizure-related injuries and ultimately the number of SUDEP.

Both undetected seizures occurred shortly after a detected GTCS. A possible explanation is that the mechanism of
muscle activation during the tonic phase of recurring GTCS is
different (smaller amplitude, shorter duration). Multiple
GTCS occurred in 7 other patients in whom all GTCS were
detected. Recurring seizures (i.e., with short interseizure pe-
riod) occurred in the group of detected seizures too. Two
of the detected, recurring seizures had interseizure periods
(73 and 74 minutes) within the range of the interseizure
periods of the undetected seizures (19–98 minutes). Thus, in
at least some patients the second GTCS might remain un-
detected, when the interseizure period is short.

Surveys of large numbers of patients and their caregivers
told the users’ requirements for wearable seizure detection
devices.7–10 Patients did not want to use implanted and EEG-
based devices. Patch electrodes at invisible body sites were
considered acceptable.7,8,10 Detection of seizures involving heavy
movement and falls was considered most important by patients
and caregivers, while for physicians, SUDEP prevention was the
most significant goal.8 This emphasizes the importance of
detecting GTCS, the seizure type that is targeted by our device.

The most important feature for users was sensitivity, with most
users requiring sensitivity over 90%. Our device provides this.
The required detection latency was under 10 seconds9 or 30
seconds.9 The median detection latency in our study was 9
seconds. In 2 cases, the muscle activation triggering the alarm
occurred 3–4 seconds before any movement was observable in
the video-EEG recordings, giving negative values for detection
latency. Concerning the FAR, the results of the surveys varied
broadly, but in all surveys users agreed that sensitivity is more
important than FAR. In one of the surveys, the acceptable FAR
was considered less than 1/wk or up to 1 false alarm/detected
seizure.9 Our device fulfilled the latter requirement, but the
overall FAR was more than 1/wk (4.7/wk). However,
throughout the study, only 2 false alarms occurred during sleep,
which is important for the quality of life of patients and
caregivers.

The baseline frequency of GTCS prior to admission to the
EMU was lower than what we recorded in the EMU. This
means that in ambulatory use, the ratio between false alarms
and true alarms would be higher than what we calculated in
the EMU, and FAR may need to be improved for ambulatory
use in medicated patients. Nevertheless, the baseline seizure
frequency of GTCS was derived from the patients’ seizure
logs, and previous studies showed that many GTCS remain
undetected by the patients.11

Device deficiency time was <5%. The device gives alarms
when the electrode impedance is too high, so that the users
can correct this. However, due to the blinding, this feature was
disabled throughout the study. Thus, it is reasonable to as-
sume that device deficiency time would be shorter when users
are alerted about this.

Two different algorithms for unimodal EMG-based seizure
detection have been developed by 2 groups. Both algorithms
have been tested retrospectively, by offline analysis of data
recorded with conventional amplifiers.17,18 Our algorithm is
generic and targets the initial phase of GTCS.17 The retro-
spective offline analysis gave a sensitivity of 100%. A modified
version of this algorithm was implemented in the wearable
device we have tested. In this prospective study, based on real-
time seizure detection, 2 of the 32 seizures were missed. This
demonstrates the importance of validating seizure detection
devices using this design, rather than by offline, retrospective
analysis. The other algorithm, developed by Brain Sentinel
(San Antonio, TX), targets a later phase: the tonic–clonic
interface.18 The algorithm is individualized and it utilizes the
Hotelling T² power analysis. The retrospective, offline analysis
showed a sensitivity of 95% (20 out of 21 GTCS from 11
patients were detected) and only 1 false alarm occurred. The
average detection latency was within 20 seconds.18 Both
algorithms have been registered for medical application: in
Europe, EDDI obtained CE registration in 2013, and Brain
Sentinel was granted de novo clearance by the Food and Drug
Administration in 2017.

In spite of numerous attempts to develop noninvasive seizure
detection,3,5 there are only 4 prospective studies on clinical val-
idation of wearable devices using real-time seizure
detection.22–25,27 All 4 studies used accelerometers. Two articles
addressed the same device: SmartWatch.26,27 Although the pilot
study showed promising results (7 out of 8 seizures were
detected),26 in a large prospective study, only 31% of GTCS
were detected.27 Another algorithm correctly identified 20 of 22
(91%) seizures from 15 patients, and had a detection latency of
17 seconds.25 Although real-time, the analysis was done on
a computer placed within 10 meters from the patient. A wearable
accelerometer device (Epi-Care Free; Tunstall, Astoria, NY)
detected GTCS with a sensitivity of 89.7%.22 Although the FAR
was low (0.2/d), this was achieved by instructing patients to
avoid movements that could trigger alarms with the arm where
the sensor was placed. The detection latency was significantly
longer (55 seconds) compared to EDDI. Accelerometers trigger
the alarm in the later, clonic phase of the GTCS, while EDDI
targets the initial part of the tonic phase, thus providing much
earlier detection (9 seconds) of the seizure and the possibility of
much earlier intervention.

The main limitation of our study is the intrinsic challenge of
any validation study of wearable seizure detection devices: the
testing was done in an EMU, which differs from the patients’
home environment. This was necessary in order to have the
reference standard. However, mobility of the patients was not
restricted during monitoring, and they were encouraged to
perform indoors physical activities similar to their habitual
lifestyle.21

Using the data recorded in this study, further optimization of
the algorithm is planned, especially for decreasing the FAR.
An alternative approach can be using individualized thresh-
olds. It is noteworthy that the device was not triggered by any
of the 14 convulsive psychogenic nonepileptic seizures that
occurred during this study, considering that all 5 patients who
had these were referred to the EMU on suspicion of GTCS. This raised the possibility of using the device for differential diagnostic purposes, as indicated previously.\(^1\)

**Author contributions**

S.B., I.C., and P.W. contributed to the conception and design of the study. S.B., O.H., and M.F. acquired and analyzed data. I.C. monitored the logs from the detection device and provided technical support. S.B. drafted the manuscript and I.C. the figures. All authors contributed to editing the manuscript.

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**Study funding**

This was an investigator-initiated study and no funding was granted to it. IctalCare, the manufacturer of the EDDI device, granted the investigators free-of-charge use of the device throughout the study period.

**Disclosure**

S. Beniczky reports no disclosures relevant to the manuscript. I. Conradsen was an employee of and is currently a consultant for IctalCare. She monitored the logs from the detection devices but did not have any influence on the logs with the time points generated by the real-time seizure detection of the device. She also gave technical assistance in form of training for IctalCare, the manufacturer of the EDDI device, granted the investigators free-of-charge use of the device throughout the study period. O. Henning, the personnel in the EMUs in using the device, but she was blinded for IctalCare. She monitored the logs from the detection device and provided technical support. S.B. drafted the manuscript and I.C. the figures. All authors contributed to editing the manuscript.

**References**


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Study question
Can the Epileptic seizure Detector Developed by IctalCare (EDDI), a wearable EMG device, provide accurate automatic detection of generalized tonic-clonic seizures (GTCSs)?

Summary answer
The EDDI device can reliably detect GTCSs.

What is known and what this article adds
Wearable seizure detectors could alert caregivers to patients’ potentially injury-inducing seizures and provide objective recording of seizure events. This study provides Class II evidence for the hypothesis that wearable EMG-based seizure detectors can provide accurate real-time GTCS detection.

Participants and setting
The study included 71 patients who had been referred to long-term video-EEG monitoring because of suspected GTCSs. The experiments were conducted in epilepsy monitoring units in Denmark and Norway between October 21, 2014, and January 23, 2017. The patients’ median baseline GTCS frequency was 1.75 per month.

Design, size, and duration
For reference data, the patients underwent video-EEG monitoring. The EDDI device was unilaterally placed over a brachial biceps muscle and was set to silently record detected seizure events. The mean recording time per patient was 53.18 hours. The EDDI seizure-detection output data were read by evaluators blinded to the relevant patient’s video-EEG data.

Main results and the role of chance
The video-EEG systems detected 32 GTCSs in 20 (28%) patients. The EDDI device detected 30 of these GTCSs for a 93.8% sensitivity (95% confidence interval 86%–100%). The 2 missed GTCSs were secondary seizures occurring after detected GTCSs. The median detection latency was 9 seconds (range −4 to 48 seconds). The false alarm rate was 0.67 per day, but 47 (66%) patients had no false alarms. Conversely, 3 (4%) patients had ≥10 false alarms. The video-EEG systems recorded 161 non-GTCS seizures, but the EDDI device did not record any of these.

Bias, confounding, and other reasons for caution
The experiment was conducted in epilepsy monitoring units, which may differ in important ways from the patients’ home environments.

Generalizability to other populations
The study focused on detecting GTCSs, so it does not establish the EDDI device’s utility for patients who experience other seizure types.

Study funding/potential competing interests
This study did not receive any funding. IctalCare granted free-of-charge use of the EDDI device. Dr. Conradsen is a former employee of and current consultant for IctalCare. Go to Neurology.org/N for full disclosures.
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