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Clinical utility of a video/audio-based epilepsy monitoring system Nelli

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ABSTRACT

Objective: The aim of this study was to evaluate the clinical utility of a semi-automated hybrid video/audio-based epilepsy monitoring system (Nelli®) in a home setting.
Methods: In this retrospective study, 104 consecutive patients underwent Nelli-registration for an average of 29 days at their home. The seizure-related data obtained from the registration were assessed to investigate the utility of the Nelli-registration regarding clinical decision-making.
Results: Of 104 patients, Nelli® hybrid system was able to recognize clinically relevant events in 83 (80%) patients: epileptic seizures in 67 (65%) and nonepileptic events in 16 (15%). A total of 2767 epileptic seizures of different seizure types were captured and identified. These seizures included not only tonic-clonic seizures but also other complex or simple motor seizures.

For the outcomes regarding clinical decision-making, a need for a new therapeutic intervention was recognized in 54 (51.9%) patients based on the number and severity of seizures captured by Nelli-registration. In 12 (11.5%) patients, the need to change the treatment plan was excluded because no evidence of suspected epileptic seizures was found. Nelli-registration aided in confirming the therapeutic efficacy of modifications of antiseizure medications (ASMs) or neuromodulation therapies in 13 (12.5%) patients. Nelli-registration enabled to determine the change in seizure classification and facilitated to reach clear diagnostic conclusions in 11 (10.6%) patients. In 14 (13.5%) patients, there was no change in clinical outcome, as Nelli-registration was unable to infer any clinical decision either due to inconclusive results or lack of typical events.

Seizures detected during Nelli-registration aided in decision-making for therapeutic interventions in 71 (68%) patients. Altogether, 44 (42%) patients had adjustment of ASMs, and in 9 (9%) patients, Nelli-registrations led to the change in the settings of vagus nerve stimulation (VNS) or deep brain stimulation (DBS) treatment. Additionally, 18 (17%) patients were referred to presurgical evaluation or established a baseline seizure frequency before surgical implantation for neuromodulation treatment with VNS or DBS, while 33 (32%) patients had no change in therapy. Nine patients (8.7%) were referred to video-EEG monitoring (VEM), as Nelli-recorded events highlighted the need for presurgical evaluation in 6 patients or further diagnostic evaluation in 3 patients.
Conclusion: This study confirms the clinical utility of the video/audio monitoring system Nelli® in home settings. Home monitoring with Nelli® hybrid system provides a new alternative for the assessment of frequency and type of epileptic seizures as well as for a recognition of nonepileptic events. Thus, Nelli-registration can facilitate the optimization of seizure monitoring and management in clinical practice, complementing existing methods such as VEM and ambulatory EEG recordings.

1. Introduction

Epilepsy is a common neurological disorder that affects approximately 65 million people globally, and over half of seizures in patients with epilepsy present with a loss of awareness [1]. Inaccurate reporting of seizure frequency is a major challenge in the treatment of epilepsy. While the standard tool for determining

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seizure frequency has been the patient/caregiver seizure diary, long-term video-EEG monitoring (VEM) studies have shown that the seizure counts reported by patients are inaccurate, and, moreover, the accuracy of seizure counts fluctuates significantly over time [2]. On average, less than 50% of all epileptic seizures are recognized using patient diaries. Furthermore, documentation as low as 15% of the true seizure count in sleep-related seizures has been reported [3]. Sleep-related generalized convulsive seizures are associated with an increased risk of sudden unexpected death in epilepsy (SUDEP), the most common epilepsy-related cause of death, and additionally, these seizures are difficult to define in terms of seizure type or seizure severity [4,5]. Moreover, seizures with hyperkinetic automatisms and/or dystonic posturing in sleep-related hypermotor epilepsy (previously nocturnal frontal lobe epilepsy), shown to originate both from frontal and extrafrontal areas, frequently mimic parasomnias with a high seizure rate [6].

Consequently, patients' ability to recall a seizure is almost always fragmentary and depends on the localization and lateralization of the seizure onset zone [3,7]. Complete recall is almost impossible, leading to underestimation of seizure frequency and misclassification of seizure types, especially in the case of seizures with impaired awareness [8]. The development of devices or systems to register objective seizure counts and characterizations would be invaluable not only for sleep-related seizures but also for seizures occurring while awake. These seizure-detection systems could enable optimal therapeutic decisions and help to evaluate the therapeutic efficacy of antiseizure medications (ASMs) or neuromodulation therapies.

Inpatient long-term VEM is the gold standard for electroclinical characterization of epileptic seizures, especially when there is diagnostic uncertainty in classifying seizure types or epilepsy syndrome. However, 20–30% of patients during VEM have nonepileptic conditions [9,10]. Prompt diagnosis is of primary importance since patients younger than 30 years of age and diagnosed with psychogenic nonepileptic seizures (PNES) on VEM have an 8-fold higher risk of death than the general population, with a similar mortality rate comparable to those with drug-resistant epilepsy [11]. Additionally, VEM may be impractical for some patients who have a low frequency of events or if seizures occur only in particular settings or during specific activities. Other factors, such as geographical limitations and transportation constraints, may restrict access to VEM, and socioeconomic conditions may hinder the availability of VEM, particularly in developing countries, thus leading to a longer delay in a definitive diagnosis [12].

Although several wearable devices have been developed to aid in counting and characterizing seizure events, these devices lack strong clinical evidence for their accuracy and are not always well tolerated, especially in children or patients with intellectual disability, thus creating a need for automated seizure detection devices, especially those capable of video monitoring at patients' homes [13]. Recently, there has been increasing interest in videos taken by family members/caregivers with smartphones, which are easy to use, cost-effective, and collect large amounts of information regarding seizure semiology for patients with multiple indications [14]. Smartphone videos may be of help in the classification of epileptic seizures as well as in the differential diagnosis of PNES [15].

The Nelli® seizure monitoring system is an audio/video-based semi-automatic (hybrid) seizure monitoring platform that uses computer vision and machine learning to identify kinematic data commonly associated with seizures with a positive motor component and human experts to visually assess these epochs [16,17]. In a recent validation study, the Nelli® hybrid system was used in a blinded setting without any prior information on the patients or their seizure types against video-EEG monitoring at a well-established epilepsy center providing accurate classification of major motor seizures including tonic–clonic, clonic, and focal motor seizures [18]. CE-marked Nelli® hybrid system has been recommended for clinical use in Finland by a government set body (the National Coordinating Group for Drug-resistant Epilepsy).

In the present retrospective study, Nelli® hybrid system home registrations were performed in the context of routine clinical practice to monitor seizures in patients with uncertainty about the true nature of suspected epileptic seizures. Registrations were conducted mostly of patients not only with a prior diagnosis but also without a prior diagnosis of epilepsy. We assessed the clinical usefulness of Nelli® hybrid system for five separate aspects: i) indications for referrals, ii) performance to properly understand and characterize seizure semiology, iii) recognition of the need for further therapeutic interventions, iv) adjustments of therapeutics during or after the use of Nelli along with the evaluation of their efficacy, and v) significance for other treatment interventions.

2. Patients and methods

In this retrospective study, 104 consecutive patients underwent Nelli-registration for an average of 29 days at their home. Although multiple registrations were performed for 34 out of 104 patients, we only reported the outcome from the first registration in the current study. This study does not require ethics committee approval according to Finnish Law on Research. Following Finnish guidelines, the study protocol was reviewed and approved by the Head of Science Centre, Tampere University Hospital Research and Innovation Services, Science Centre (Reference code R16522). The study included patients from one university hospital with a dedicated epilepsy center and three regional hospitals with general neurologists. All patients undergoing routine clinical care for epilepsy-related disorders were retrospectively identified and enrolled following routine chart reviews at Tampere University Hospital, Seinäjoki Central Hospital, Vaasa Central Hospital, and Rovaniemi Central Hospital.

Indications for using Nelli® hybrid system were further categorized (Table 1), with modifications as suggested by Shih et al. [19].

The Nelli® seizure monitoring system consists of a specialized video camera/microphones that can be set up in home or hospital settings to detect nocturnal seizures or seizures occurring in a distinct location, such as sofas where patients spend a significant amount of their time. Biomarkers extracted algorithmically create analyzable entities from optical flow/audio data from prospective recordings of clinically relevant events. The Nelli® hybrid system automatically removes periods of inactivity and saves periods that include abnormal motor/audio activity. Next, Nelli® hybrid system annotators with video-EEG technician training reviewed the algorithmic findings and provided a report of the true seizure count, including predicated seizure types with descriptions of seizure

Table 1
Indications for video monitoring with Nelli® hybrid system.

		Indications
1.		**Determine whether spells are epileptic seizures (spell classification or differential diagnosis)**
2.		**Determine seizure semiology**
	a.	*Identify the type of seizures occurring in individuals with known epilepsy (seizure classification)*
	b.	*Monitor seizure frequency (seizure quantification) for evaluation of need for further clinical intervention*
3.		**Adjust treatment interventions to control seizures**
	a.	*Medication adjustment*
	b.	*Neuromodulation treatment (VNS/DBS) adjustment*

DBS: deep brain stimulation; **VNS**: vagus nerve stimulation.

clusters as well as the frequency, intensity, and duration of the events.

Different types of seizures that were recorded during Nelli-monitoring were grouped into three main seizure categories: focal aware motor seizures (FAMS), focal impaired awareness motor seizures (FIAMS), and focal to bilateral tonic-clonic seizures (FBTCS)/-generalized tonic-clonic seizures (GTCS) [20]. The results, including a written report comprising technologist annotations, were reviewed by the treating physician applying the interactive user interface. Electronic patient files were reviewed for assessment of relevant clinical history, including therapeutic changes in ASMs or neuromodulation therapies. The clinical utility of the Nelli-registration was categorized to prespecified utility measures:

a. ***Outcomes enabling clinical decision-making*:** change in seizure classification (differential diagnostics), the need for therapeutic intervention either confirmed or excluded based on presence or absence of epileptic seizures, therapeutic efficacy of prior changes in either ASMs or neuromodulation confirmed, and no effect on clinical outcomes (unsuccessful registration).
b. ***Therapeutic interventions*:** adjustment of ASMs, referral to presurgical evaluation or establishment of a seizure baseline prior to surgical implantation for neuromodulation treatment with vagus nerve stimulation (VNS) or deep brain stimulation (DBS), change in the settings of VNS or DBS treatment, and no change in treatment or diagnosis.

3. Results

3.1. Baseline characteristics

Demographic information of the study population is summarized in Table 2. Most patients who had a prior diagnosis of epilepsy had focal epilepsy. The study population was being treated following standard of care practices prior to monitoring; more than half of the patients registered (52%) had previously undergone VEM. Before Nelli-monitoring, the patient-reported seizure frequency was variable. The frequency of weekly seizures was higher than that of daily or monthly seizures, while only four patients reported annual seizures.

Table 2
Demographic data for patients using Nelli® hybrid system.

Background characteristics	
N	104
Age, mean (range)	33 (16–78)
Sex (F/M)	58/46
Intellectual disability, n	33
Prior Diagnosis of epilepsy, n	92
Epilepsy type, n	
Focal	80
Generalized	3
Unknown	9
Epilepsy syndrome or topography, n	
TLE	11
XLE	30
Multifocal	19
Focal Unclassified	20
IGE	1
CAE	1
Generalized Unclassified	1
Patient-Reported Seizure Frequency before Monitoring	
Daily	21
Weekly	49
Monthly	21
Annually	4
Unknown	11
Days of Nelli monitoring mean (range)	29 (7–43)

CAE: childhood absence epilepsy; **IGE**: idiopathic generalized epilepsy; **TLE**: temporal lobe epilepsy; **XLE**: extra-temporal lobe epilepsy.

3.2. Indications for Nelli-registrations

Patients may have had multiple indications for Nelli-registrations. In 42% of patients, the indication included spell classification or differential diagnosis (Table 1; *1*). Most (88%) of the patients were monitored to better classify and quantify their seizures (Table 1; *2a and 2b*, respectively). The indication in 24% of patients was to register the effectiveness of a change in ASMs, and in 15% of patients the indication for Nelli-registration included the evaluation of the effects of parameter changes in neuromodulation devices (Table 1; *3a and 3b*, respectively).

3.3. Events captured during Nelli-registration

The total number of monitoring days for all 104 patients was 2965 days (mean 28.5 days). Nelli® hybrid system was able to recognize spells in 83 (80%) patients: 67 (65%) had epileptic seizures, and 16 (15%) had nonepileptic events. The remaining 21 (20%) patients did not have any significant events recorded.

3.3.1. Epileptic events captured by Nelli® hybrid system

During Nelli-registration, in 67 patients with documented epileptic events, the total number of seizures captured was 2767. Thirty-four patients had a total of 1400 FAMS, and 52 patients had a total of 1350 FIAMS. Six patients had in total 17 FBTCS/GTCS. Seizure types and frequencies during the whole Nelli-registration period are presented in Table 3.

3.3.2. Non-epileptic events captured by Nelli® hybrid system

Nelli-monitoring identified nonepileptic events in 16 patients: nonepileptic arousals in 8 patients, nonepileptic muscle cramps in 2 patients, myoclonic jerk (hypnagogic jerk) in 1 subject, parasomnia episodes in 2 patients, and PNES in 3 patients. Notably, 2 out of 16 patients had epileptic events in addition to nonepileptic events.

3.4. Patient-reported seizure frequency prior to registration

The number of seizures, that patients reported prior to monitoring with Nelli, was compared to the number of seizures that was identified during the monitoring period. Seventy-two of the patients reported that they experienced seizures outside of sleep or were unsure about when seizures occurred, while 32 of the patients reported only having seizures during periods of rest. When comparing patient-reported seizure frequencies on a categorical level (daily, weekly, monthly, annually), 25% of the patients were able to accurately predict the number of events that were registered during Nelli-registration. Almost half of the patients (47%) with sleep-related seizures only predicted that they would have more seizures than were identified during monitoring. Twenty-two percent predicted that they would have fewer seizures than were identified with Nelli-registrations. Patients who were unable to estimate their seizure frequency were categorized as "unknown", although their seizure frequency was established during monitoring. Table 4 summarizes patient-reported seizure frequency compared to the frequency of seizures that were identified during monitoring with Nelli® hybrid system.

3.5. Clinical utility measures of Nelli-registration

3.5.1. Outcomes enabling clinical decision-making

Outcomes from Nelli-registration were categorized into five different categories (Fig. 1). For the outcomes regarding clinical

Table 3
Seizure types and frequencies during Nelli-monitoring.

Seizure types	Seizure sub-categories	Patients (*n*)	Total Seizures (*n*)	Median (range)
FAMS				
	FAMS (unspecified)	29	1307	125 (1–832)
	FAMS myoclonic	2	60	30 (17–43)
	FAMS tonic	2	26	13 (9–17)
	FAMS clonic	1	7	
FIAMS				
	FIAMS (unspecified)	17	612	8 (1–146)
	FIAS hyperkinetic	21	535	18 (1–190)
	FIAS automatisms	8	111	6.5 (3–49)
	FIAS tonic	5	90	10 (6–49)
	FIAS clonic	1	2	
FBTCS/GTCS				
	FBTCS/GTCS	6	17	-

FAMS: focal aware motor seizures; **FIAMS:** focal impaired awareness motor seizures; **FBTCS:** focal to bilateral tonic clonic seizures; **GTCS:** generalized tonic-clonic seizure.

Table 4
Accuracy of patients-reported seizure frequencies.

	Sleep-related seizures only (*n* = 32)	Seizures outside of sleep (*n* = 72)
Over-report (%)	47	30
Under-report (%)	22	22
Accurate (%)	25	34
Unknown (%)	6	14

Over-report: patients reporting more seizures than were recorded; **Under-report:** Patients reporting fewer seizures than were recorded; **Accurate**: patients reported seizures that were consistent with the Nelli-detected seizures; **Unknown:** patients are unaware or unknown of seizure occurrence.

decision-making, a need for a new therapeutic intervention was recognized in 54 (51.9%) patients based on the number and severity of seizures captured by Nelli-registration (first outcome). Conversely, in 12 (11.5%) patients, the need to change the treatment plan was excluded because no evidence of suspected epileptic seizures was found (second outcome). Therefore, there was no change in ASMs during or after the registration period. Six out of these 12 patients did not have a prior diagnosis of epilepsy. Nelli-recognized findings in these six patients were as follows: two had no typical events captured, and in four patients, nonepileptic events (unspecific arousals, parasomnias, and unspecific movements) were detected. In these patients, the follow-up was terminated after the exclusion of active epileptic seizures. Furthermore, Nelli-registrations helped to confirm the therapeutic efficacy of ASMs or neuromodulation in 13 (12.5%) patients (third outcome).

Nelli-registration enabled to determine the change in seizure classification and facilitated treating physician to reach a clear diagnostic conclusion in 11 (10.6%) patients (fourth outcome). One patient who did not have a diagnosis of epilepsy prior to registration was confirmed with the diagnosis of epilepsy (frontal lobe epilepsy based on seizure semiology) during the period of registration. Pre-existing epilepsy diagnosis was confirmed in six patients. The presence of PNES was documented in one patient and additionally in another patient, the coexistence of epileptic seizures and PNES was found. Two patients' sleep-related events were confirmed as nonepileptic.

The fifth outcome was 'no change in clinical outcome' in all 14 (13.5%) patients because the Nelli-registration did not help to infer any clinical decision. Eight patients did not have significant events detected during the Nelli registration, and in 6 patients, the registration results were inconclusive.

3.5.2. Therapeutic interventions after Nelli-registration

Nelli enabled therapeutic intervention in 68% (71/104) of the patients after registration (Fig. 2). The most common intervention was the adjustment of ASMs. In 17% (18) of patients, registration led to a referral to presurgical evaluation (3 patients) or the establishment of a baseline seizure frequency prior to surgical implantation for neuromodulation treatment with VNS or DBS (15 patients). Nelli-registration led to a change in the settings of VNS or DBS treatment in 9% (9) of the patients. One-third of patients did not require therapeutic interventions.

When analyzing specific therapeutic interventions with reference to the aforementioned outcomes enabling clinical decision-making (Section 3.5.1), the following observations were made:

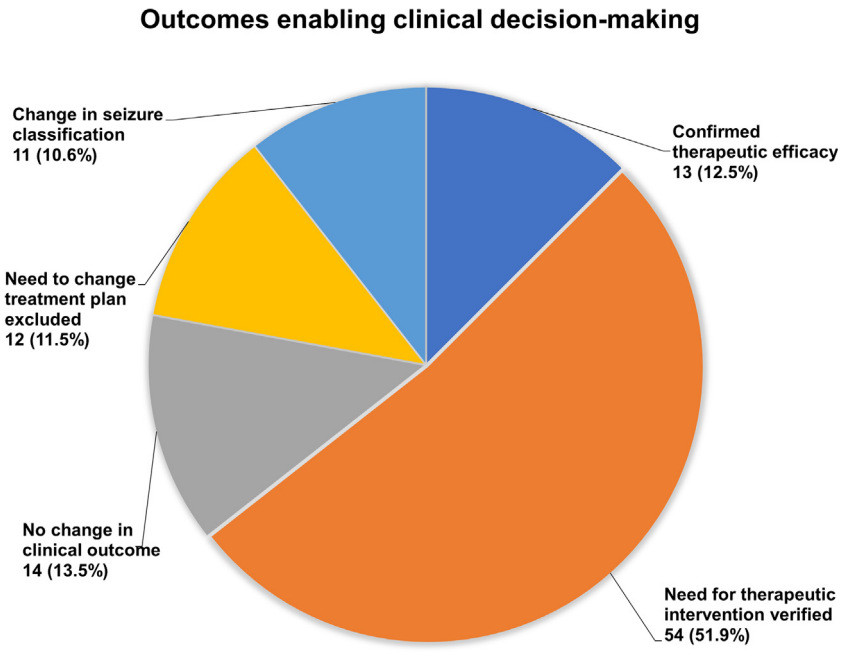

Fig. 1. Outcomes of Nelli-registration on clinical decision-making.

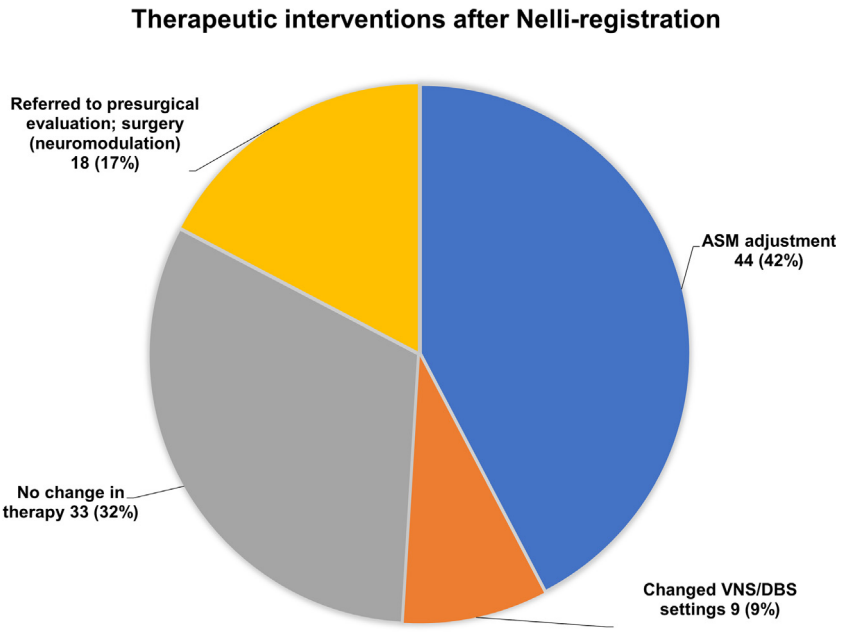

Fig. 2. Therapeutic interventions after Nelli-registration.

i) Out of 54 patients with a newly recognized need for therapeutic intervention, ASMs were adjusted in 27 patients, VNS/DBS settings were changed for 10 patients, and for the remaining 17 patients, registration led to referral to presurgical evaluation or the establishment of a baseline prior to surgical implantation for neuromodulation treatment with VNS or DBS.
ii) Among 11 patients in whom a change in seizure classification (differential diagnosis) was determined, four had ASM adjustment, while seven had no change in therapy. The reasons for no change in therapy were either the suspected events turned out to be nonepileptic, thus excluding the need for change in therapy (three patients), or the suspected events were confirmed to be epilepsy, but there was no need to change therapy because the seizures were nondisabling (four patients).
iii) Among 13 patients, in whom the therapeutic efficacy of ASMs or changes in neuromodulation parameters were confirmed, 11 patients underwent further ASM adjustment. Two patients had no change in therapy because there was no need for therapeutic adjustment after the registration period, as the patients were seizure free during Nelli-registration after the ASM adjustment.

3.5.3. The duration of Nelli-registration in patients without typical events or inconclusive results

The median (range) duration of Nelli-registration in patients without typical events or inconclusive results was 28 (15–43) and 28 (16–33) days, respectively.

3.6. Need for VEM after Nelli-registration

Out of 104 patients, 95 (91%) patients did not require VEM after the use of Nelli. However, for 9 (9%) patients, VEM was performed. Three patients needed VEM for a diagnostic purpose (the results of Nelli-registration were inconclusive), and 6 patients needed VEM for presurgical evaluation due to recognition of disabling seizures based on Nelli-registration results. The VEM outcomes for the first 3 patients (VEM for diagnostic purposes) were as follows: the first patient had a successful withdrawal of ASM and overturned prior epilepsy diagnosis, the second patient had a confirmed epilepsy diagnosis with generalized epilepsy, and the third patient was currently pending referral. The VEM outcomes for the remaining 6 patients (VEM for presurgical evaluation) were as follows: two patients were referred to a resective surgery program, one was considered for neuromodulation therapy, another did not have seizures during VEM, and two patients' referrals were still pending.

4. Discussion

Video-based long-term registrations in the home setting provide a new alternative for accurate assessment of the frequency and type of epileptic seizures as well as for recognition of nonepileptic events. This study provides evidence for the clinical utility of the video/audio-based seizure recognition Nelli-system for achieving clinically meaningful information in 86% of the registered patients and for providing the basis for therapeutic adjustments in 68% of patients. Nelli® hybrid system was able to recognize clinically relevant events in 83 (80%) of the registered patients. Of those, 67 patients had epileptic seizures, and 16 had nonepileptic events. Nelli-registrations complement existing methods for seizure evaluation, such as standard seizure diaries, smartphone videos, and VEM registrations in an epilepsy monitoring unit (EMU).

In this study, we monitored patients who were typically young and had a diagnosis of refractory seizures, while a third of them had intellectual disabilities. Regardless of the epilepsy type, these patients generally experienced seizures with impaired awareness, were not able to keep reliable diaries, or were not able to recall events due to cognitive issues. Independent of the underlying reason, these patients referred for Nelli-registration were not able to provide their treating physician with data that are essential to properly understand seizure semiology, monitor treatment effectiveness, or assess the progression of seizure-related disorders. Most of the patients had focal epilepsy, especially extratemporal lobe or multifocal epilepsy. There were fewer patients with generalized epilepsy. It is well established that especially in frontal lobe epilepsy (representing most of the extratemporal lobe group in our study), seizures occur more frequently or exclusively during sleep, both during the day and night [21].

There were three basic indications for referrals to undergo a Nelli-registration [19]. First, patients were monitored for differential diagnosis with or without a prior diagnosis of epilepsy but with uncertainty regarding whether the current seizures were epileptic, nonepileptic, or both. Nelli-registration enabled us to differentiate the events, facilitating the diagnostic and therapeutic decisions in most of the registrations. Second, most of the patients were indicated for Nelli-registration to identify the type and frequency of seizures occurring in individuals with known epilepsy, termed seizure classification as well as seizure quantification. The third indication was the evaluation of treatment interventions to control seizures with either ASM adjustments or neuromodulation (VNS/DBS) treatment adjustments. The comparison of indications for Nelli-registrations with indications for VEM or other proposed devices was not the primary aim of this study. However, the use of Nelli appeared to have broader indications, especially in terms of its utility in the evaluation of treatment interventions with either ASM adjustments or neuromodulation (VNS/DBS) treatment adjustments, compared to outpatient smartphone videos or ambulatory VEM recordings [10,15]. The use of smartphone videos is mainly indicated for the differential diagnosis of paroxysmal neurologic events and for the diagnostic evaluation of PNES [15,22,23] and for picking up semiological signs for classifying seizure types [24]. However, smartphone videos lack diagnostic certainty, as the ILAE Nonepileptic Seizures Task Force recommends that home video recordings can only be used as an add-on to the diagnostic evaluation for PNES [9].

There are few devices that are cleared by regulatory bodies to identify tonic-clonic seizures, and only two provide objective data for clinical review [25]. In the present study, not only tonic-clonic seizures but also other motor seizures, such as FAMS and FIAMS, were identified and classified based on Nelli-registrations. The distinction between aware and impaired awareness seizures was based on information from prior investigations (such as video EEG) and clinical history included in the referral.

According to our recent validation study the Nelli® hybrid system was able to provide accurate classification of motor seizures including tonic–clonic, clonic, and focal motor seizures [18]. The semiology of these seizures could also be further characterized to include descriptions of automatisms, clonic, hyperkinetic, myoclonic, and tonic activity. The ability for trained epileptologists to have access to this level of data would aid in the diagnostic characterization of seizure events and may supplement current standards of practice in the care of patients with paroxysmal events. Paroxysmal disturbances of cerebral function are best diagnosed with correlated clinical behavior and simultaneous EEG; however, clinicians experienced in the diagnosis of seizure disorders can clinically establish semiological features of events with video alone. Capturing events with VEM or even video alone may be difficult due to the unpredictable nature of seizure events, and a patient or caregiver's subjective recollection of events may not be particularly useful. Patients with frequent night-time seizures and convulsive tonic-clonic seizures are at a higher risk of injury and potentially SUDEP, which highlights the importance of prompt diagnosis [11]. With the objective video data that Nelli provides, epilepsy specialists may be able to stratify their patients with epilepsy into important risk categories and optimize individual treatment plans [17]. This study essentially shows how therapies were adjusted when treating clinicians had access to video of events without having to monitor patients in a hospital environment.

As the most common clinical utility of Nelli-registration, Nelli® hybrid system helped to recognize the necessity of therapeutic intervention for more than half of the patients registered. Conversely, in another group of patients, there was a suspicion of seizures, but the results of Nelli-registration confirmed that no interventions were required. In patients with confirmed epilepsy, the need for therapeutic intervention was already more likely based on prior clinical information for a patient continuing to have seizures, although the Nelli system may add quantitative data. Change in seizure classification was a meaningful outcome that Nelli provided to clinicians to help validate different seizure types. The most common finding related to the therapeutic changes during or after Nelli was the adjustment of ASMs. Patients who had no change in clinical outcome were referred to as the patients for whom the registration was inconclusive because it did not lead to any specific outcomes, or the results of the registration did not help to develop any clinical decision.

Antiseizure medications often have undesirable side effects. Current options for monitoring the therapeutic efficacy of ASMs are limited because seizure diaries are often unreliable. Nelli-home monitoring was useful for the patients, as their treating physicians were able to witness the nature and frequency of events objectively, often for the first time in the patient history. The information provided by Nelli-registration allowed physicians to optimize ASMs or neuromodulatory treatments, which otherwise may have not been possible. Currently, VNS and DBS operating parameters are often adjusted based only on patient-reported outcomes.

Without an electrographic correlate, video monitoring may not be sufficient to replace VEM in some patients but may still assist in the screening of patients for the optimized utilization of EMU and ambulatory EEG studies. Usefulness of ambulatory EEG devices in the management of epilepsy has been reported in several studies. These devices enable the detection of not only epileptiform activity but also helps to classify and quantify seizures and epilepsy syndromes [26–28]. In our cohort, nine patients were referred for VEM because the events recorded with Nelli highlighted the need for presurgical evaluation or further diagnostic evaluation. Clinically significant results were achieved for these nine patients as VEM outcomes. Although this study does not include young children, recognizing epileptic seizures in such a population without VEM would be invaluable [29].

Patients have a high acceptance for automated seizure registration if it has a minimal negative effect on daily living and therefore multiple wearable devices are on the market [30]. However, their utilization is limited due to a lack of standard clinical validation in medical decision-making. There have been no safety-related concerns identified during the post-market use of Nelli® hybrid system. Since the camera never comes into patient contact during monitoring and there are no interventions that are driven by Nelli's ability to identify events, there are little, or no risks associated with its use. Thus, our findings strengthen the evidence of the clinical usefulness of Nelli-registrations and ensure sufficient measures of safety standards.

This study also has some limitations. The retrospective nature of the study and data collected only from a single registration limit the applicability of our results. Additionally, the generalizability of the study results depends on the characteristics of the patient populations analyzed. Moreover, in this feasibility-type retrospective study, no control group was included, which limits the possibility for comparison with clinical practice without Nelli-registrations. Since the Nelli-system can register only seizures with alterations in motor activity, patients with nonmotor seizures cannot be evaluated. In the validation study of the Nelli® hybrid system, there was lower accuracy in classifying more discrete motor seizures such as myoclonic jerks, short tonic seizures, and epileptic spasms [18]. On the other hand, the validation study included also children and adolescents [18], but the present retrospective study only included patients aged 16 or older, in which these seizure types are less common. Although multiple registrations were performed for some patients, we only reported the outcome from the first registration. The duration of registration with any given system has a

significant impact on capturing relevant events, and a longer registration offers a greater likelihood of capturing events of varied characteristics, especially if there is more than one type of event. Comparing the results from the first registration to the subsequent registrations could have provided additional information on the significance of Nelli use. The probability of detecting seizures depends upon the frequency of baseline events and the duration of the monitoring period [31]. For instance, capturing events through 3–5 days of VEM monitoring may not be sufficient to detect real seizure counts. Therefore, these home-video registrations could help to evaluate the optimal duration of VEM registrations, particularly if there are infrequent seizures, then longer registrations may help to capture those seizures such as a single seizure in a duration of a single month.

5. Conclusions

Inaccurate subjective seizure count generates treatment and diagnostic challenges in everyday clinical practice; therefore, our findings from real-world clinical utilization of Nelli-registration help to fill this gap. Nelli-registration may offer clinicians a possibility of a more detailed view of the nature and frequency of paroxysmal events and/or seizures in patients with epilepsy. The ability for the provider and the patient/caregiver to review events together with the treating physician opens opportunities for becoming more involved and informed in treatment decision-making and increases the possibility of recognizing potential changes in diagnosis/prognosis over time. We have presented a significant number of patients in whom the use of VEM resources could be optimized because Nelli-registration-derived clinical information was sufficient for meaningful clinical decision-making. Moreover, Nelli-monitoring in the home setting is vital during situations such as lockdown during the coronavirus disease pandemic when patients cannot visit outpatient clinics or hospitals for VEM recordings.

Declaration of interests

JP is one of the founders and shareholders of Neuro Event Labs, manufacturer of the Nelli device. Rest of the authors report no disclosures.

Ethics approval and consent to participate

This study does not require ethics committee approval according to Finnish Law on Research. Following Finnish guidelines, the study protocol was reviewed and approved by the by the Head of Science Centre, Tampere University Hospital Research and Innovation Services, Science Centre (Reference code R16522).

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None.

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