



## The use and yield of continuous EEG in critically ill patients: A comparative study of three centers



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### HIGHLIGHTS

- Analysis of 5700+ records at three high-volume centers show a similar pattern of continuous EEG use.
- Rate of identification of seizures and time to first seizure detection and periodic patterns are nearly identical.
- Differences in antiseizure drug use suggest discrepancies in how cEEG results influence management.

### ABSTRACT

**Objective:** Continuous EEG (cEEG) monitoring of critically ill patients has gained widespread use, but there is substantial reported variability in its use. We analyzed cEEG and antiseizure drug (ASD) usage at three high volume centers.

**Methods:** We utilized a multicenter cEEG database used daily as a clinical reporting tool in three tertiary care sites (Emory Hospital, Brigham and Women's Hospital and Yale – New Haven Hospital). We compared the cEEG usage patterns, seizure frequency, detection of rhythmic/periodic patterns (RPP), and ASD use between the sites.

**Results:** 5792 cEEG sessions were analyzed. Indication for cEEG monitoring and recording duration were similar between the sites. Seizures detection rate was nearly identical between the three sites, ranging between 12.3% and 13.6%. Median time to first seizure and detection rate of RPPs were similar. There were significant differences in doses of levetiracetam, valproic acid, and lacosamide used between the three sites.

**Conclusions:** There was remarkable uniformity in seizure detection rates within three high volume centers. In contrast, dose of ASD used frequently differed between the three sites.

**Significance:** These large volume data are in line with recent guidelines regarding cEEG use. Difference in ASD use suggests discrepancies in how cEEG results influence patient management.

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## 1. Introduction

Continuous electroencephalogram (cEEG) provides a non-invasive method to monitor brain function in real time in critically ill patients (Alvarez and Rossetti, 2015). Most of the seizures in

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patients with disorders of consciousness are non-convulsive and the yield of cEEG in detecting non-convulsive seizures has been well described (Claassen et al., 2004; Abend et al., 2013). This has led to the increasingly widespread use of cEEG in neurocritically ill patients. The American Clinical Neurophysiology Society (ACNS) and the European Society of Intensive Care Medicine (ESICM) have recently published recommendations regarding cEEG indications (Herman et al., 2015a; Claassen et al., 2013). Despite its obvious advantages, variability in the use of cEEG has been recently described in a survey of neurologists (Abend et al., 2010).

In order to standardize the clinical practice of critical care EEG monitoring, the ACNS has adopted a standard terminology for EEG patterns encountered in these patient (Hirsch et al., 2013), with repeated inter-rater reliability studies and modifications (most recently (Gaspard et al., 2014)). The Critical Care EEG Monitoring Research Consortium (CCEMRC), a consortium affiliated with the ACNS, promotes research and quality improvements in the use of EEG in critically ill patients and has developed a database based on this terminology serving as both a collaborative data sharing mechanism and repository, and as a daily practice reporting tool (Lee et al., 2016). Three large volume centers, the Brigham and Women's Hospital (BWH), Boston, MA, USA; Emory University Hospital (Emory), Atlanta, GA and the Yale-New Haven Hospital (Yale), New Haven, CT, USA have utilized it for daily use for all critically ill patients undergoing cEEGs.

The aim of the present study is to describe and compare the current use and yield of cEEG across three large volume centers in daily practice to provide a reference base for emerging centers implementing cEEG monitoring.

## 2. Methods

### 2.1. Primary research question

Describe and compare cEEG use and its yield in critically ill patients

### 2.2. Cohort

All three centers used this database daily for all cEEG as part of routine clinical reporting starting at the BWH (February 2013), Emory (August 2013), and Yale (October 2013). We extracted data from the central database on September 30, 2015. Patients at the BWH and Emory included all patients who underwent an inpatient cEEG recording for >1 h, both in the intensive care units as well as the ward services; at Yale, all patients in the intensive care units and ward patients were entered. All data were entered by clinical neurophysiologists, epilepsy specialists, or clinical fellows who were familiar with the ACNS terminology and had passed a detailed certification test (Gaspard et al., 2014).

### 2.3. Definition of variables

The following data were collected: (1) patient's age and gender (2) cEEG specifications: clinical indication, duration (if the cEEG was interrupted but reapplied within 48 h, it was considered part of the same recording session), use of video, use of quantitative analysis; (3) cEEG findings: seizure identification rate, seizure type (non-convulsive seizure, focal seizure, generalized convulsive seizure and seizure with subtle clinical signs only), time to first seizure, presence of periodic and/or rhythmic patterns according to the 2012 ACNS terminology (Hirsch et al., 2013) (4) Patient management: anti-seizure drug (ASD) use during cEEG. The doses of the four most commonly used ASDs (levetiracetam, lacosamide,

valproic acid, and phenytoin/fosphenytoin) were analyzed; the maximum daily dose for a particular recording session was extracted. Due to their similarities, the use and doses of phenytoin and fosphenytoin were combined for analysis. For more details see database description (Lee et al., 2016).

### 2.4. Standard protocol approvals

The institutional review boards of each center approved this study and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. As this observational study involved no risk for patients, and focused on acutely ill subjects, consent was waived.

### 2.5. Statistical analysis

Continuous variables were described by mean and standard deviation, or median and the inter-quartile range, depending on the variables' distributions. Categorical variables were described by frequencies. The three hospital groups were compared using  $\chi^2$ , Wilcoxon rank-sum, student *t*-tests, ANOVA or Kruskal–Wallis test, as required. Results with a *p*-value < 0.05 were considered statistically significant. Due to the large number of subjects per group, size-effect was assessed using Cramer's Phi ( $\Upsilon$ ) test or  $\eta^2$  ( $\eta^2$ ) as required. Cramer's  $\Upsilon$  < 0.1 were considered as negligible effect, 0.1 to 0.3 as small, 0.3 to 0.5 as medium and > 0.5 as large effect.  $\eta^2$  < 0.01 were considered as negligible, 0.01 to 0.06 as small, from 0.06 to 0.14 as medium and > 0.14 as large effect (Ellis, 2010). Multiple comparisons testing was performed via the False Discovery Rate (Benjamini et al., 1995) set at 0.2. Tests were performed using STATA 13 (StatCorp – College Station – Texas, USA) and Matlab R2015b (Mathworks, Natick, MA).

## 3. Results

During the study period, 5792 cEEG's from 4889 unique patients in three centers were identified: Emory: 1994 (34.5%), BWH: 2012 (34.8%) and Yale: 1786 (30.9%).

Technical specifications and clinical indications are shown in table 1. Median cEEG duration was significantly longer at Emory (30 h compared with 24 h for BWH and Yale), however, the effect size was negligible ( $\eta^2 = 0.002$ ). Duration of monitoring of comatose patients (median 45.2 h) was longer than non-comatose patients (24.2 h) at each of the 3 sites, with significant differences between the sites, but a negligible effect size. In the three sites, video and quantitative EEG were used during most recordings with a smaller use of both features at Yale. BWH and Emory used video in >95% of recording while Yale used it in 86.7%. The difference was significant ( $p < 0.001$ ), but the effect size was small (Cramer  $\Upsilon$ : 0.14). Video and qEEG were omitted at each institution only when there were resource limitations (recording devices not equipped with camera or qEEG software in some instances) or equipment failure; the default policy was to record video and perform qEEG on all studies (see Fig. 1 for qEEG example). Emory used quantitative EEG (qEEG) for nearly all recordings (98.5%) and BWH and Yale used it less frequently, but still for the majority of patients (83.8% and 81.2% respectively), the difference was significant ( $p < 0.001$ ), but the effect size was small (Cramer  $\Upsilon$ : 0.23). There were also significant differences in patient's demographics across the three centers: The median age was approximately 60 years old in the three sites and about half of the patients were female but with a negligible effect size ( $\eta^2 = 0.01$  for age and Cramer  $\Upsilon = 0.03$  for gender). Regarding clinical indications for cEEG (table 1), the most frequent

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