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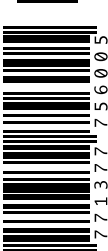
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EEG measures continuously at the bedside the human brain's electrical activity. Its main advantages are noninvasiveness, good spatial and temporal resolution, and sensitivity to changes in both brain structure and function.

In ICU, seizures are frequent in patients with/without acute brain injury. They are often difficult to recognise, because they are non-convulsive. This provides support in favour of continuous EEG (cEEG) rather than "spot" EEG, typically for a period of less than 30 minutes. cEEG refers to the recording of EEG over extended time periods in critically ill patients at risk for secondary brain injury and neurologic deterioration. Unfortunately, intensivists aren't usually trained in interpreting EEG, due to difficulties in interpretation of the recordings. Usually a neurophysiologist's consult is required. For this reason, EEG has been usually recorded on the spot, and it has not been deemed a potentially useful tool for continuous monitoring of the damaged brain, except in some neurological institutions. Fortunately, times are changing.

Indications for Continuous EEG Recording in ICU

Several guidelines recommend the use of cEEG in the ICU setting (Claassen et al. 2013; Le Roux et al. 2014; Claassen and Vespa 2014; Herman et al. 2015) for:

1. The diagnosis of nonconvulsive seizures (NCS) and nonconvulsive status epilepticus (NCSE). NCSE is a state of continuous/repetitive seizures without convulsions. Due to the nonspecific signs and significant morbidity and mortality associated with NCSE, research has focused on early diagnosis and seizure

Quantitative EEG in ICU

Useful and Feasible

termination. Standard EEG misses identifying NCSE in more than 75% of cases. Instead cEEG (lasting 6-12 hours or longer) is able to identify up to 80% of NCSE (Friedman et al. 2009). NCS are associated with such secondary insults as increased intracranial pressure, reduction in tissue oxygenation, and local metabolic derangements. Therefore, even if the effect of NCS identification and management on outcome has not been fully proven, untreated NCS is associated with increased mortality and increased risk for poor neurologic outcome. Therefore early identification of NCS with cEEG in patients with unexplained altered level of consciousness is strongly recommended (Sutter et al. 2016).

2. The assessment of efficacy of therapy for seizures and status epilepticus, when sedation and high-dose suppressive therapy, after first-line therapies, are required.

3. The identification of cerebral ischaemia. cEEG could detect delayed cerebral infarction in subarachnoid haemorrhage patients before clinical deterioration and CT scan changes become evident. In fact, the reduction of the ratio between alpha (8-13 Hz) and delta (<4 Hz) frequency, with an increase in slow frequencies, is becoming an interesting application of cEEG (Claassen et al. 2004; Rots et al. 2016).

4. The expansion of multimodality monitoring (MMM) of the injured brain, adding continuous information on the function of the cerebral cortex and its metabolic and functional variations. Advanced MMM should integrate neurophysiological information with neuroimaging and different continuous physiologic data, such as ICP, CPP, and PbtO₂, with EEG-derived parameters (Citerio et al. 2015).

Barriers and Possible Solutions for Implementing cEEG in ICU

Even if the indications are rather clear, ICU practice is far from a diffuse implementation of cEEG. Barriers to its implementation

are here summarised, along with possible solutions for overcoming these obstacles:

- **Limited availability of EEG technicians and neurophysiologists to review the studies 24/7.**

In the UK, for example, a survey documented that only a minority of ICU units (33%) have access to continuous EEG monitoring, despite it being considered fundamental for patients' management (Patel et al. 2015). In a larger USA survey, continuous EEG is more frequently utilised (Gavvala et al. 2014). However, a substantial interhospital variability has been described. In a single centre study, only a minority (27%) of critically ill patients presenting criteria for EEG monitoring had an EEG recording (Park and Boyd 2015).

A possible solution is the integration of ICU staff in the continuous evaluation of the EEG recording. In our unit, after a standard EEG, EEG technicians position the electrodes with ICU nurses' help. Nurses have been trained to check the recording hourly and to reposition the electrodes if not working and to use a transparent dressing for stabilising the electrodes over time. Daily check of the system is planned by neurophysiologist technicians. Neurophysiologists discuss with ICU doctors the indications for monitoring and, on a daily basis, discuss the 24-hour recordings with ICU staff. ICU doctors and residents, present 24/7, have been trained to identify the most significant patterns utilising derived parameters as quantitative EEG (see below).

- **Lack of uniform terminology and of consensus on the clinical significance of selected EEG patterns.**

Neurophysiologists defined some criteria (Leitinger et al. 2015) for NCS identification, but variability in EEG interpretation still remains (Rodriguez Ruiz et al. 2016). Intensivists using cEEG need to focus on important items, i.e. outcome-related patterns. In our experience, we targeted to identify during the cEEG monitoring phase:

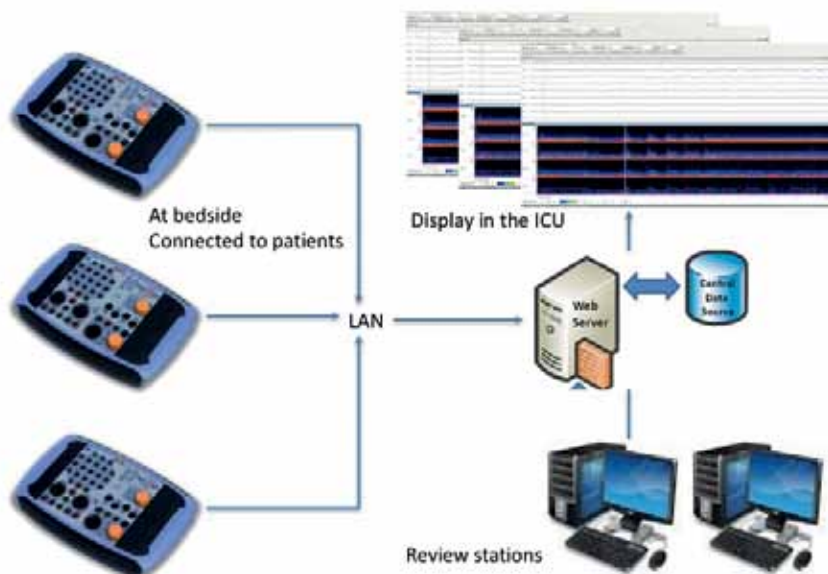


Figure 1.

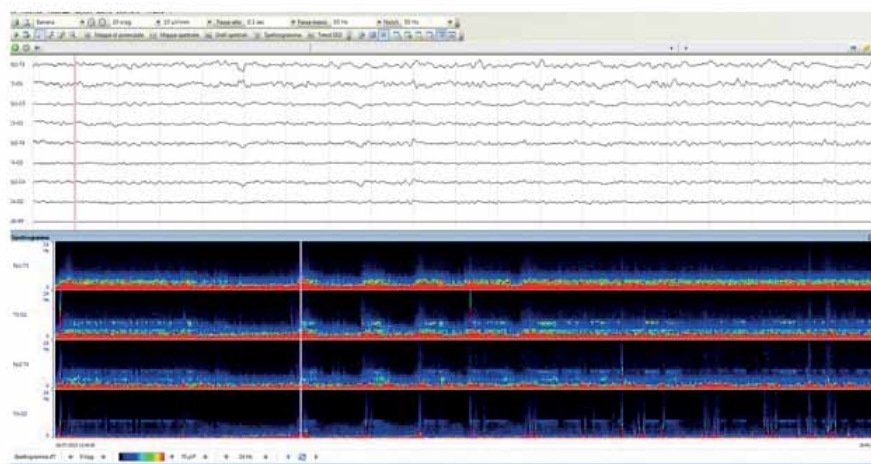


Figure 2.

- Artefacts
 - Seizures
 - Sedation level
 - Asymmetry
- **Need for an infrastructure for cEEG in a busy modern ICU environment.**

Ideal tools are cheap, small, capable of being fully networked, with the possibility to review the recording in several locations. **Figure 1** presents the setting actually used in the San Gerardo Neurointensive Care Unit. Several small EEG patients' units are networked. In the ICU, the recordings are displayed at nursing and medical stations. Review stations, two in the ICU offices and the third in the neurophysiologists' offices, are available. All the data are stored on a dedicated server.

- **Huge amount of recorded EEG-data requires time for reviewing and interpretation.** Quantitative EEG (qEEG), could reduce the time required for reviewing hours of recordings (Haider et al. 2016). However, it is imperative to summarise and simplify: qEEG, defined by the American Academy of Neurology (Nuwer 1997) as “*the mathematical processing of digitally recorded EEG in order to highlight specific waveform components, transform the EEG into a format or domain that elucidates relevant information, or associate numerical results with the EEG data for subsequent review or comparison*”, could help intensivists in reaching this aim. The huge amount of data is “digested” by a computer and summarised in a more accessible format. After a learning period, typical patterns, such as seizures, could be easily identified by non experts.

If we want to utilise cEEG as a monitoring tool, continuous evaluation of these recordings is needed. Moreover, for making the monitoring useful in the patient's care plan, intensivists, while detecting a pathological condition (i.e. seizures or oversedation), have to react, modifying their therapeutic approach.

Intensivists using cEEG need to focus on outcome-related patterns

Implementation of qEEG: Summary of Our Experience

We studied the implementation of qEEG in our Unit in the clinical trial *Continuous Quantified EEG in NeuroIntensive Care (CrazyEEG)*, NCT02901262 (clinicaltrials.gov/ct2/show/NCT02901262), following these steps:

Phase 1. Definition of a cEEG recording setting.

The neurophysiologists and the intensivists defined a common setting for the study. Continuous EEG was recorded using 8 electrodes arranged according to the 10-20 International System, on a bipolar longitudinal montage plus a ground and a reference electrode.

Our c/qEEG setting includes:

- Continuous raw EEG tracings, useful for the neurophysiologist check of the Density Spectral Array (DSA) data,
- DSA is an EEG power-based display used to convey the frequency and power distribution of the EEG signal over time.
- Amplitude-integrated EEG (aEEG). Amplitude-integrated EEG expresses the amplitude compressed on a logarithmic scale of the EEG with an upper margin and a lower margin showing the highest and the lowest amplitude of EEG in a time period. It represents the collective electrical energy of neuronal firing
- Burst suppression rate (BSR), measuring the amount of time within an interval spent in the suppressed state. This ratio increases as the brain becomes progressively less active, and it is an indicator of pharmacological suppression intensity.

Figure 2 depicts a raw EEG (30 sec) and

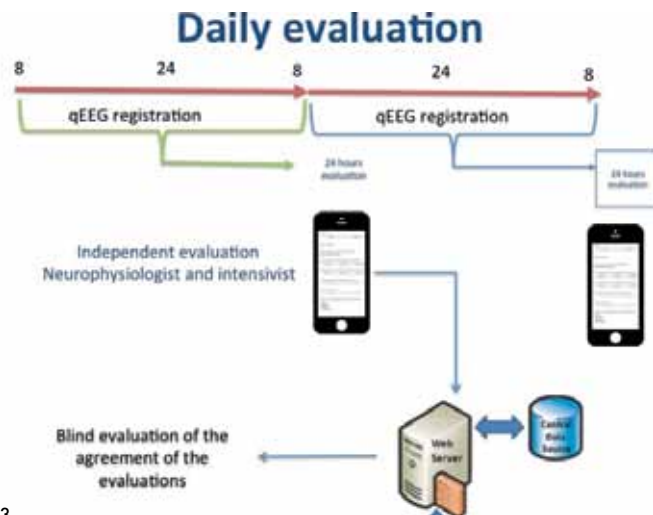


Figure 3.

the qEEG of the last 24 hours of recordings in the same patient. In the bottom part of the figure, the Density Spectral Array (DSA) is obtained from raw data using a Fourier transformation that gives the power contained within the various frequency bands, and is represented on a x-y graph that shows the time on the x axis and colours corresponding to the power at different frequencies on the y axis.

cEEG was recorded accordingly to the previously presented guidelines, including unexplained neurological status based on clinical history and imaging, frequent seizures and status epilepticus suspicion and management.

Phase 2. Baseline evaluation and neurophysiology training.

Intensivists were exposed to online training using the Clinical Electroencephalography for Anesthesiologists presentation developed by Purdon and Brown at Massachusetts General Hospital (<https://iii.hm/7x4>).

We anonymously tested the baseline knowledge on qEEG after the online course using a

web-based system. Ten recordings with the display defined in step 1 were randomly presented. We evaluated the ability to:

1. assess the depth of sedation
2. evaluate symmetry between the hemispheres
3. recognise seizures and
4. recognise artefacts

The responses from intensivists were compared to those of two experienced neurophysiologists, used as “gold standard”. We were disappointed after this step. Intensivists were not so good in interpreting qEEG.

After the baseline test, the intensivists received formal neurophysiology training consisting of lectures and discussion with the neurophysiologist of the recorded qEEG, integrating qEEG data with the clinical status and management strategies of the patients.

Phase 3. Check of the interpretation of qEEG after a 6-month learning period.

We compared qEEG evaluation by intensivists with the neurophysiologists’ interpretation after 6 months of exposition and daily

discussion. An app was developed for this aim (Figure 3). Every 12-24 recording period has been evaluated by the intensivist and by the neurophysiologist independently and blindly. We compared the responses after the first 25 patients.

The depth of sedation was correctly evaluated by intensivists in 90.7% of cases, artefacts in 95.3% of cases, symmetry in 81.4% of cases and seizures in 80.2% of cases.

Conclusions

The implementation of a qEEG system, supported by frequent interaction with a neurophysiologist, boosted the use of cEEG in our ICU.

ICU physicians cannot fully substitute for a neurophysiologist. Nevertheless, if they focus on clinically relevant questions (i.e. presence of seizures) they can gain sufficient knowledge to identify potentially dangerous conditions and for starting timely treatment. ■

Conflict of Interest

Giuseppe Citerio declares that he has no conflict of interest.

Abbreviations

aEEG	amplitude-integrated EEG
cEEG	continuous EEG
BSR	Burst suppression rate
c/qEEG	continuous quantitative EEG
CPP	cerebral perfusion pressure
DSA	Density Spectral Array
EEG	electroencephalogram
ICP	intracranial pressure
MMM	multimodality monitoring
NCS	nonconvulsive seizures
NCSE	nonconvulsive status epilepticus
PbtO ₂	partial pressure of brain tissue oxygen
qEEG	quantitative EEG

References

- Citerio G, Oddo M, Taccone FS [2015] Recommendations for the use of multimodal monitoring in the neurointensive care unit. *Curr Opin Crit Care*, 21(2): 113-9.
- Claassen J, Hirsch LJ, Kreiter KT et al. [2004] Quantitative continuous EEG for detecting delayed cerebral ischemia in patients with poor-grade subarachnoid hemorrhage. *Clin Neurophysiol*, 115(12): 2699-710.
- Claassen J, Taccone FS, Horn P et al. [2013] Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM. *Intensive Care Med*, 39(8): 1337-51.
- Claassen J, Vespa P. Participants in the International Multi-disciplinary Consensus Conference on Multimodality Monitoring [2014] Electrophysiologic monitoring in acute brain injury. *Neurocrit Care*, 21 Suppl 2: 129-147.
- Friedman D, Claassen J, Hirsch LJ [2009] Continuous electroencephalogram monitoring in the intensive care unit. *Anesth Analg*, 109(2): 506-23.
- Gawala J, Abend N, LaRoche S et al; Critical Care EEG Monitoring Research Consortium [CCEMRC] [2014] Continuous EEG monitoring: a survey of neurophysiologists and neurointensivists. *Epilepsia*, 55(11): 1864-71.
- Haider HA, Esteller R, Hahn CD et al. [2016] Sensitivity of quantitative EEG for seizure identification in the intensive care unit. *Neurology*, 87(9): 935-44.
- Herman ST, Abend NS, Bleck TP et al. [2015] Consensus statement on continuous EEG in critically ill adults and children, part I: indications. *J Clin Neurophysiol*, 32(2): 87-95.
- Le Roux P, Menon DK, Citerio G et al. [2014] Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. *Intensive Care Med*, 40(9): 1189-209.
- Leitinger M, Beniczky S, Rohrachner A et al. [2015] Salzburg consensus criteria for non-convulsive status epilepticus - approach to clinical application. *Epilepsy Behav*, 49: 158-163.
- Nuwer M [1997] Assessment of digital EEG, quantitative EEG, and EEG brain mapping: report of the American Academy of Neurology and the American Clinical Neurophysiology Society. *Neurology*, 49(11): 277-292.

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