

New technology: refractory status epilepticus

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Updates in technology & treatment modalities

- SE guidelines review
- Diagnostic technology
 - quantitative EEG analysis
 - automatic seizure detection
- Emerging treatment modalities
 - therapeutic hypothermia
 - neurostimulation: VNS, DBS, TMS, RNS
 - electroconvulsive treatment

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

Epilepsia, 56(10):1515–1523, 2015
doi: 10.1111/epi.13121

“a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t1). It is a condition, which can have long-term consequences (after time point t2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.”

Operational dimensions

- T1 – prolonged seizure
- T2 – risk of damage

	T1	T2
Tonic-clonic	5	30
Focal	10	> 60
Absence	10-15	unknown

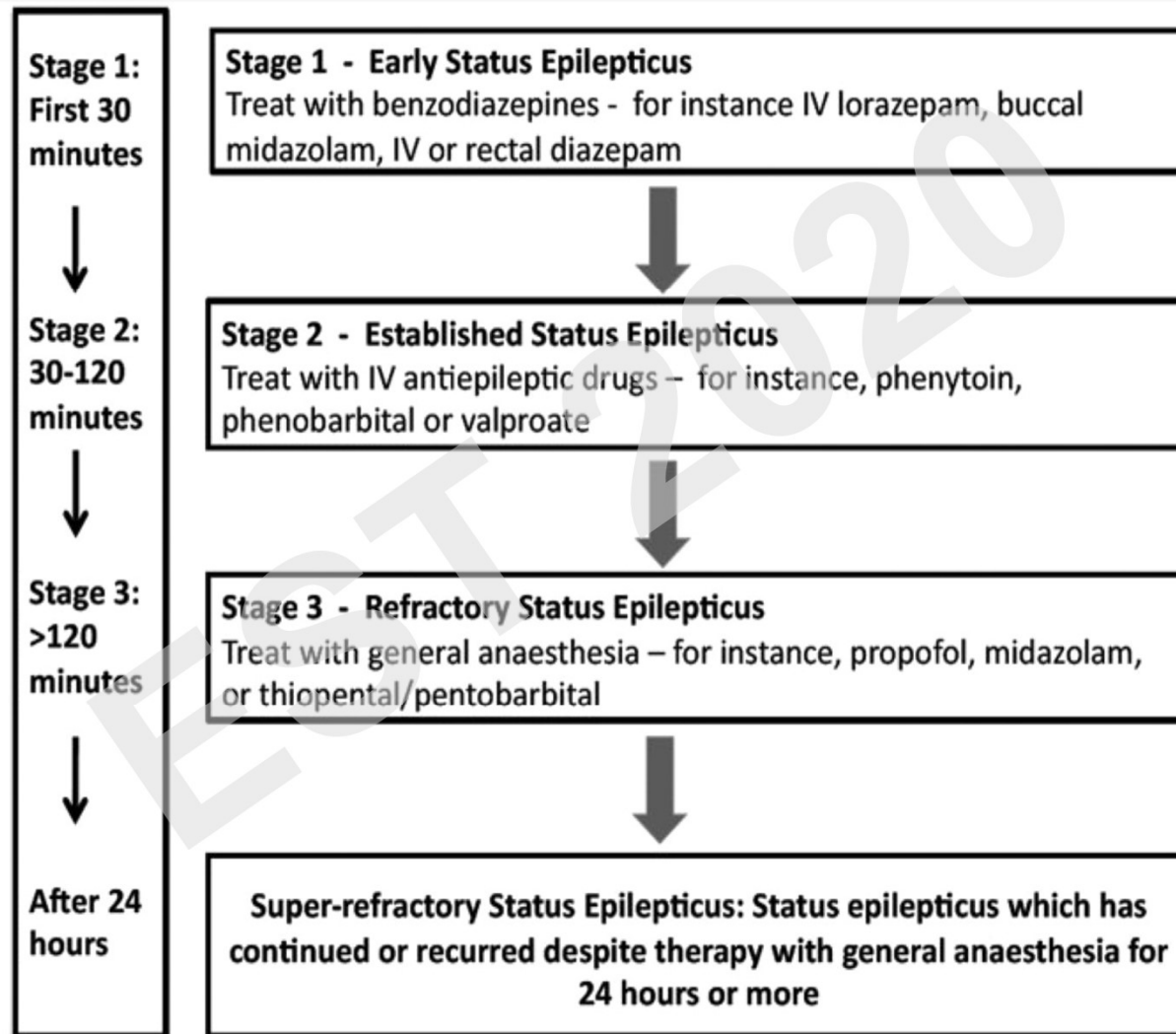
Treatment guidelines

- NICE 2011
- AES 2016
- Thai 2016
- Others

→ Similar approach

→ Different intervention time and drug dose

Stages of SE

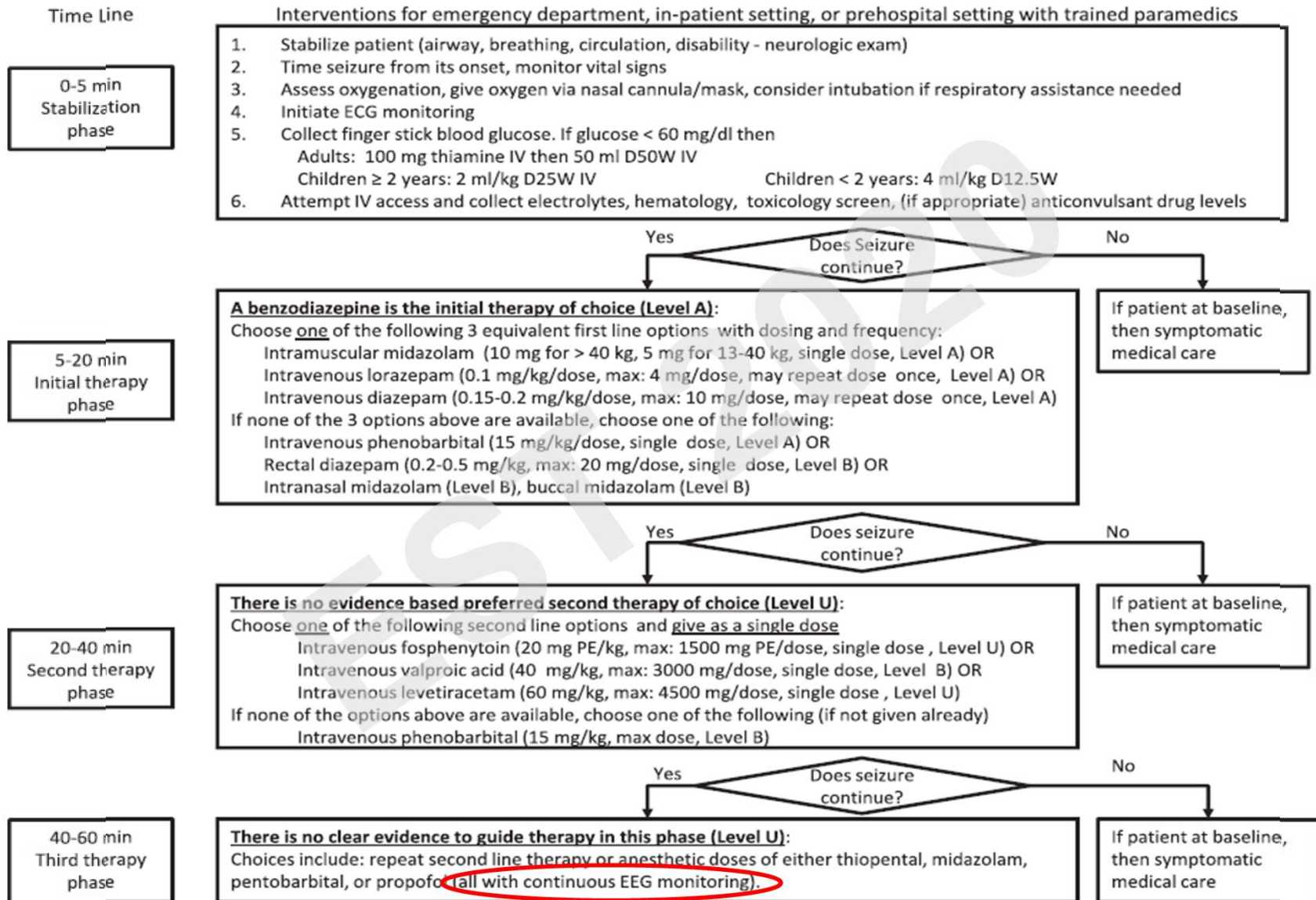


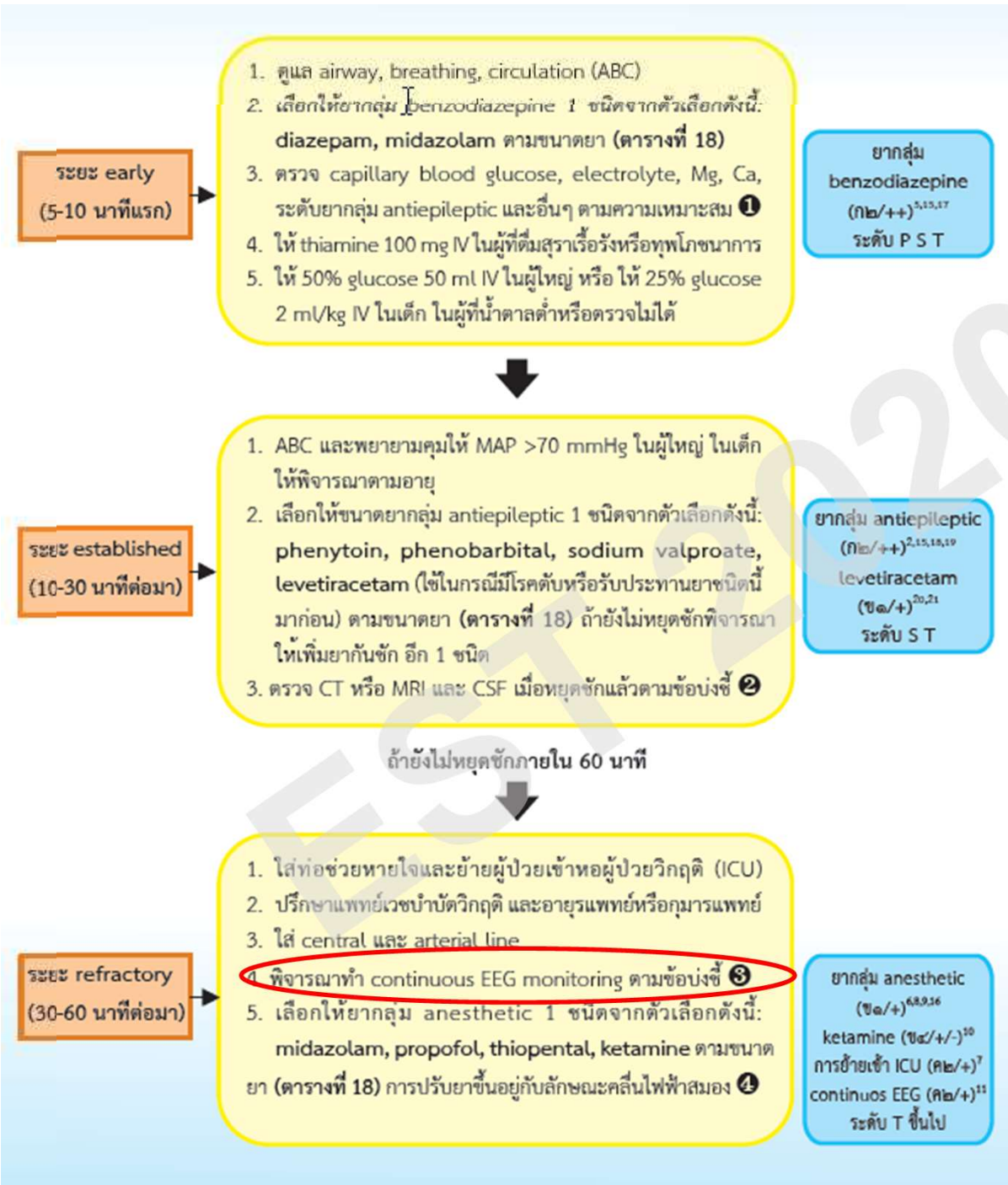
The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol. Brain. 2011;134(10):2802-2818

NICE

Time	Seizure starts	Confirm clinically that it is an epileptic seizure
0 mins (1ststep)	Check ABC, high flow O₂ if available Check blood glucose	
5 mins (2ndstep)	Midazolam 0.5 mg/kg buccally or Lorazepam 0.1 mg/kg if intravenous access established	Midazolam may be given by parents, carers or ambulance crew in non-hospital setting
15 mins (3rdstep)	Lorazepam 0.1 mg/kg intravenously	This step should be in hospital Call for senior help Start to prepare phenytoin for 4 th step Re-confirm it is an epileptic seizure
25 mins (4thstep)	Phenytoin 20 mg/kg by intravenous infusion over 20 mins or (if on regular phenytoin) Phenobarbital 20 mg/kg intravenously over 5 mins	Paraldehyde 0.8 ml/kg of mixture may be given after start of phenytoin infusion as directed by senior staff Inform intensive care unit and/or senior anaesthetist
45 mins (5thstep)	Rapid sequence induction of anaesthesia using thiopental sodium 4 mg/kg intravenously	Transfer to paediatric intensive care unit

AES





Thai CPG

Thai CPG

ในระยะ refractory continuous status epilepticus ③

พิจารณาทำ EEG monitoring ในผู้ป่วยดังต่อไปนี้

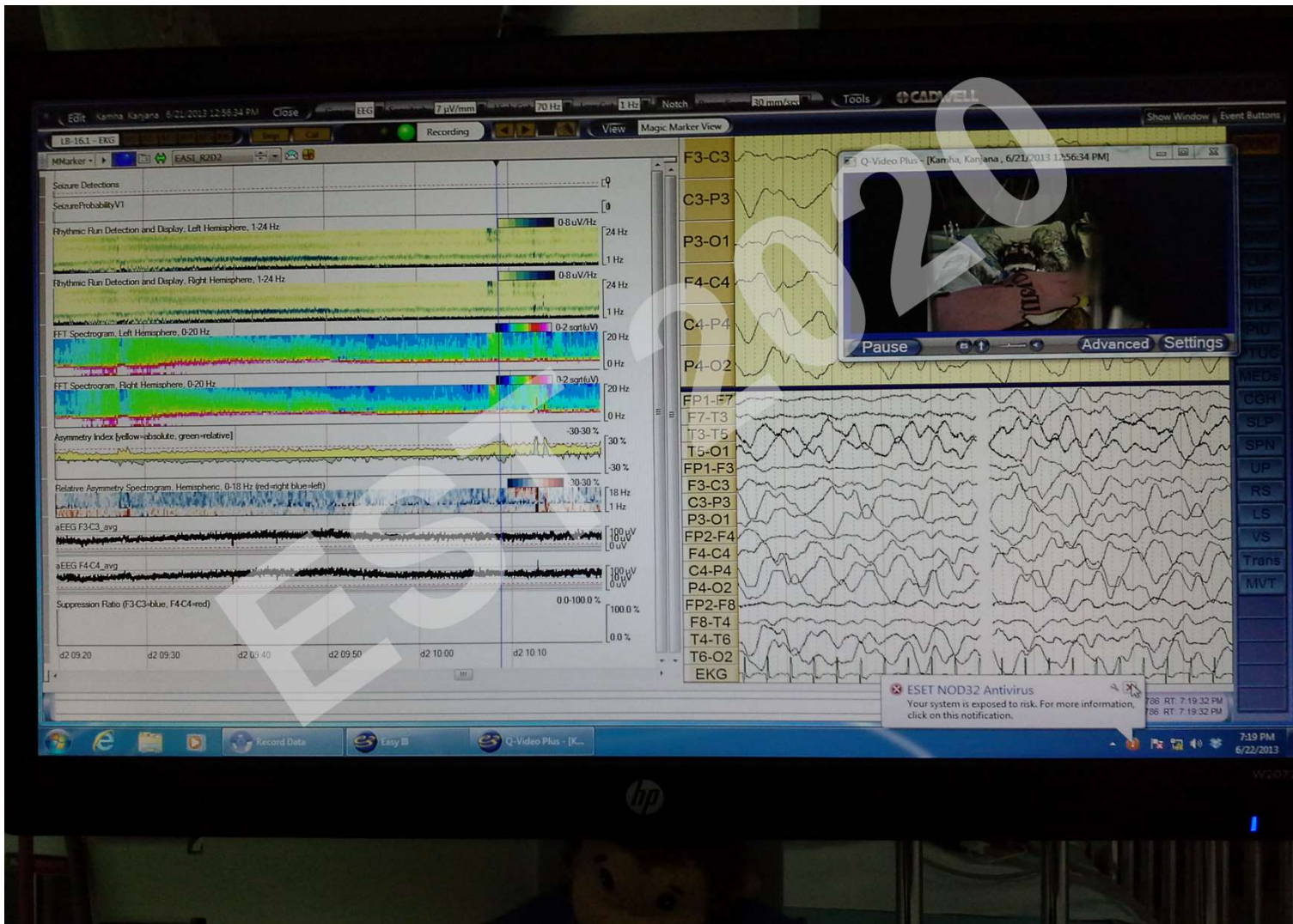
1. ยังมีอาการชักอยู่ เนื่องจากต้องใช้คลื่นไฟฟ้าสมองเป็นตัวประเมินการให้ยากกลุ่ม anesthetic agents
2. หยุดชักได้แล้วแต่ผู้ป่วยยังไม่รู้สึกตัวภายใน 24 ชั่วโมง (ผู้ป่วย convulsive SE หลังหยุดชักสามารถพบ

ภาวะ non-convulsive SE หรือ subclinical SE ได้ร้อยละ 20)

การปรับขนาดยากกลุ่ม anesthetic agents ④

การปรับขนาดยากกลุ่มนี้จะดูตามการเปลี่ยนแปลงของคลื่นไฟฟ้าสมองบน continuous EEG monitoring โดยเป้าหมายหลักในการใช้ยากกลุ่มนี้ คือ 1) หยุด seizure activity ร่วมกับ 2) คลื่นไฟฟ้าสมองมีลักษณะเป็น burst suppression (ประกอบไปด้วย burst ซึ่งมีลักษณะ high amplitude polymorphic activity และ interburst ซึ่งมีลักษณะเป็น suppression) ควบคุมให้ระยะเวลา interburst interval อยู่ในช่วง 5-15 วินาทีต่อเนื่องเป็นระยะเวลา 24 ชั่วโมง

cEEG



Why qEEG ?

- cEEG – 24 h at 15 s/page = 5760 pages
 - Monitoring SRSE can last several days
- Problem



qEEG analysis

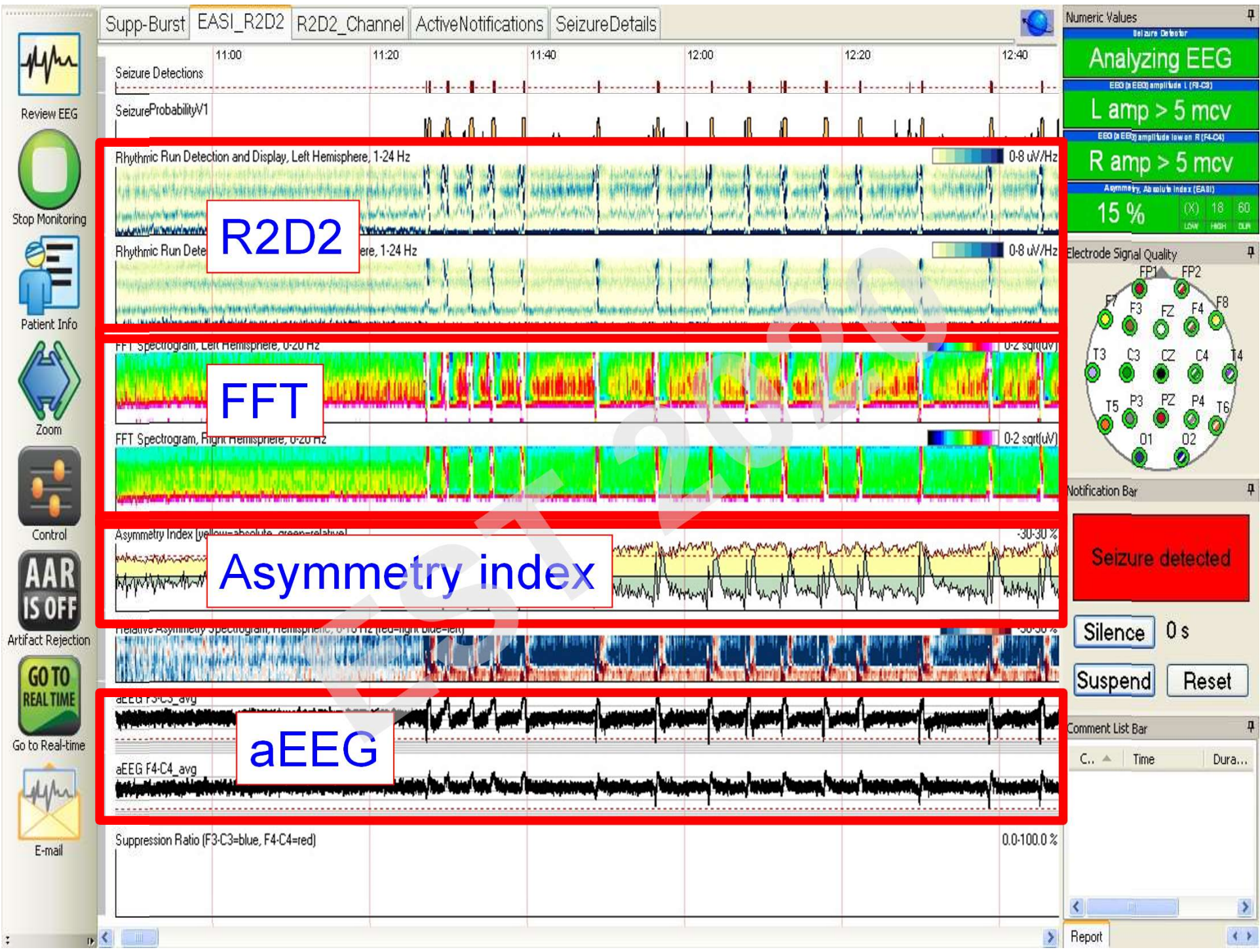
- parameters calculated for a brief epoch of EEG data
 - Then plotted versus time
 - Less reviewer's burden
 - Easy pattern recognition for on-site doctors
- Allow preliminary interpretation

Time-domain analysis

- how EEG amplitude varies over time
- Amplitude-integrated EEG (aEEG)
- Envelope Trend Analysis
- Burst suppression ratio (BSR)

Frequency-domain analysis

- Fourier analysis (or spectral analysis)
- Power (amplitude squared (r^2) of the Fourier series)
- Compressed Spectral Array
- Power Ratios
- Asymmetry Index (power in a given frequency band in the right VS left)
- Rhythmic Spectrogram



R2D2

FFT

Asymmetry index

aEEG

Numeric Values

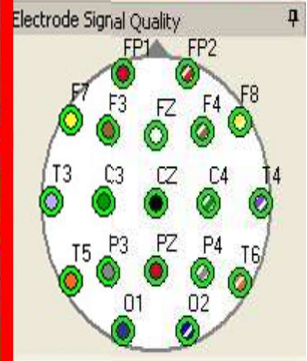
Seizure Detector

Analyzing EEG

EEG (aEEG) amplitude L (F3-C3)
L amp > 5 mcv

EEG (aEEG) amplitude low on R (F4-C4)
R amp > 5 mcv

Asymmetry, Absolute Index (EAI)
15 % (X) 18 60
LOW HIGH CLR



Seizure detected

Silence 0 s

Suspend Reset

Comment List Bar

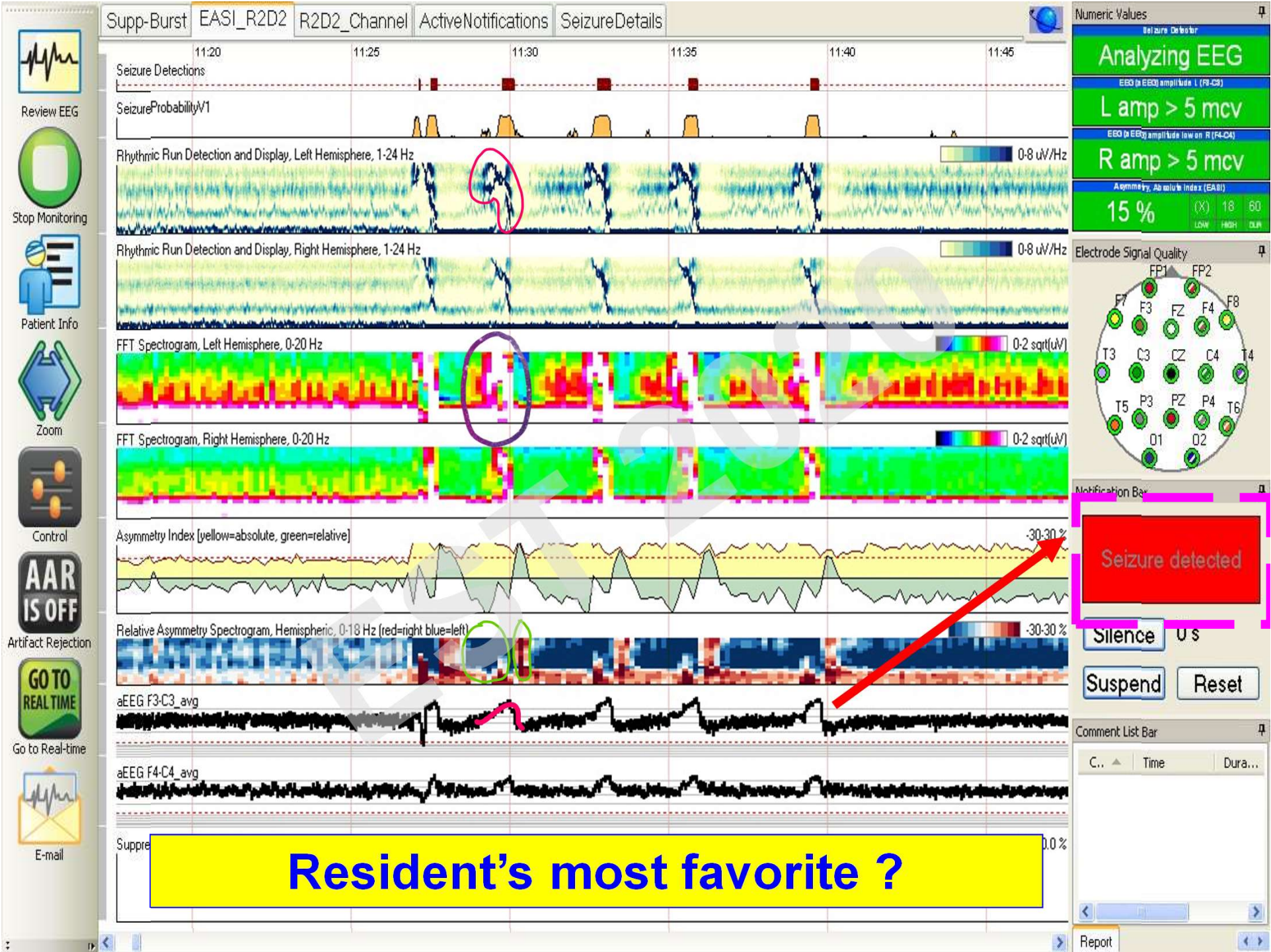
C. Time Dura...

Report

qEEG & Sz detection

- Change in amplitude/ frequency/ rhythmicity
- Sensitivity 41-89%
- False positive rate 5-39
- Accuracy affected by many variables

→ Better used as a screening to selectively review raw EEG



Resident's most favorite ?

automated seizure detection

- Raw EEG processed by various algorithms
- Sensitivity 33-93%
- Commercial software (persyst 12)
→ Sensitivity 76%, false positive rate 0.9/h
- Accuracy affected by many variables

qEEG example

- 11 years old girl
 - intractable epilepsy
 - on LVT, TPM, Clobazam
 - Phenytoin allergy
-
- tonic Sz 1-2 /week
 - today - Sz increased to 20-30/d



Return MM



Stop Monitoring



Patient Info



Zoom



Control



Artifact Rejection



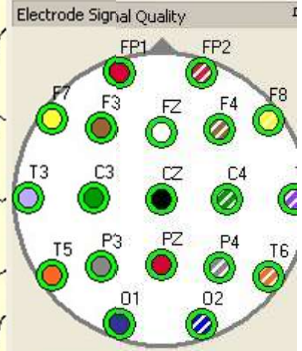
Go to Real-time



E-mail



Training



Notification Bar

Silence 0 s

Suspend Reset

Comment List Bar

Time s G... Channel

Montage 10 uV 1 Hz 70 Hz 50 On

Spikes Bursts Bookmarks R

BP-Longitudinal

Numeric Values



Return MM



Stop Monitoring



Patient Info



Zoom



Control



Artifact Rejection



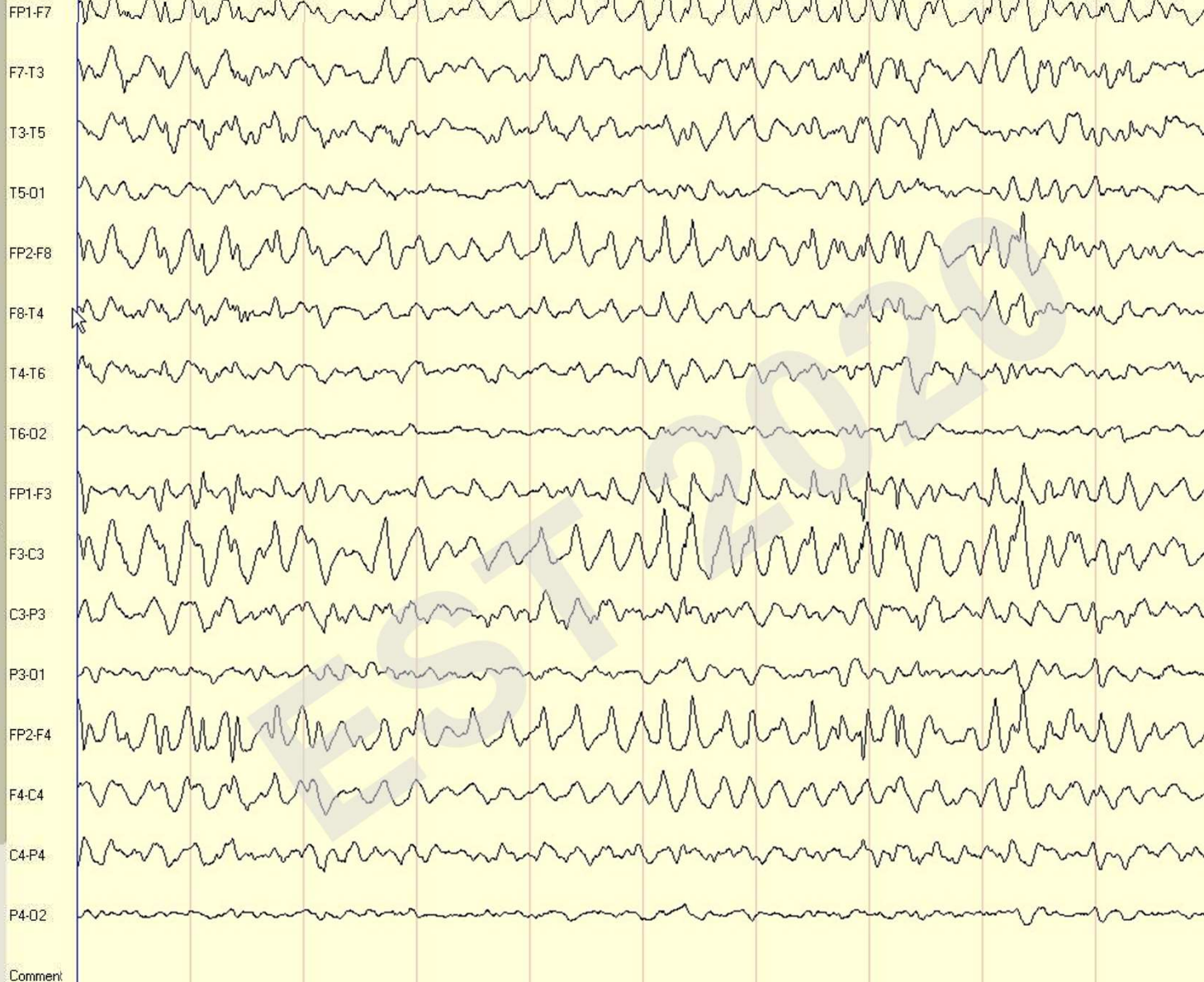
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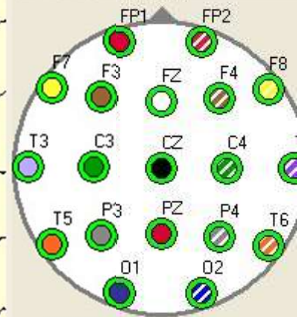
E-mail



Training



Electrode Signal Quality



Notification Bar



Silence 0 s

Suspend Reset

Comment List Bar

Time s G... Channel

Montage 10 uV 1 Hz 70 Hz 50 On

Spikes Bursts Bookmarks R

Return MM

Stop Monitoring

Patient Info

Zoom

Control

AAR IS OFF

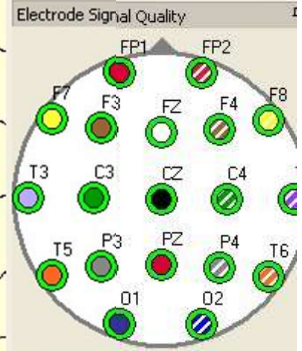
Artifact Rejection

GO TO REALTIME

Go to Real-time

E-mail

Training



Notification Bar

Silence 0 s

Suspend

Reset

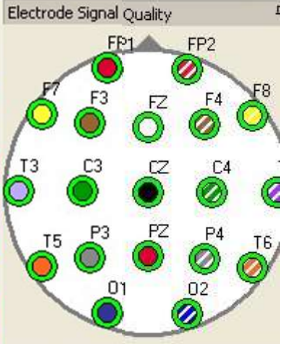
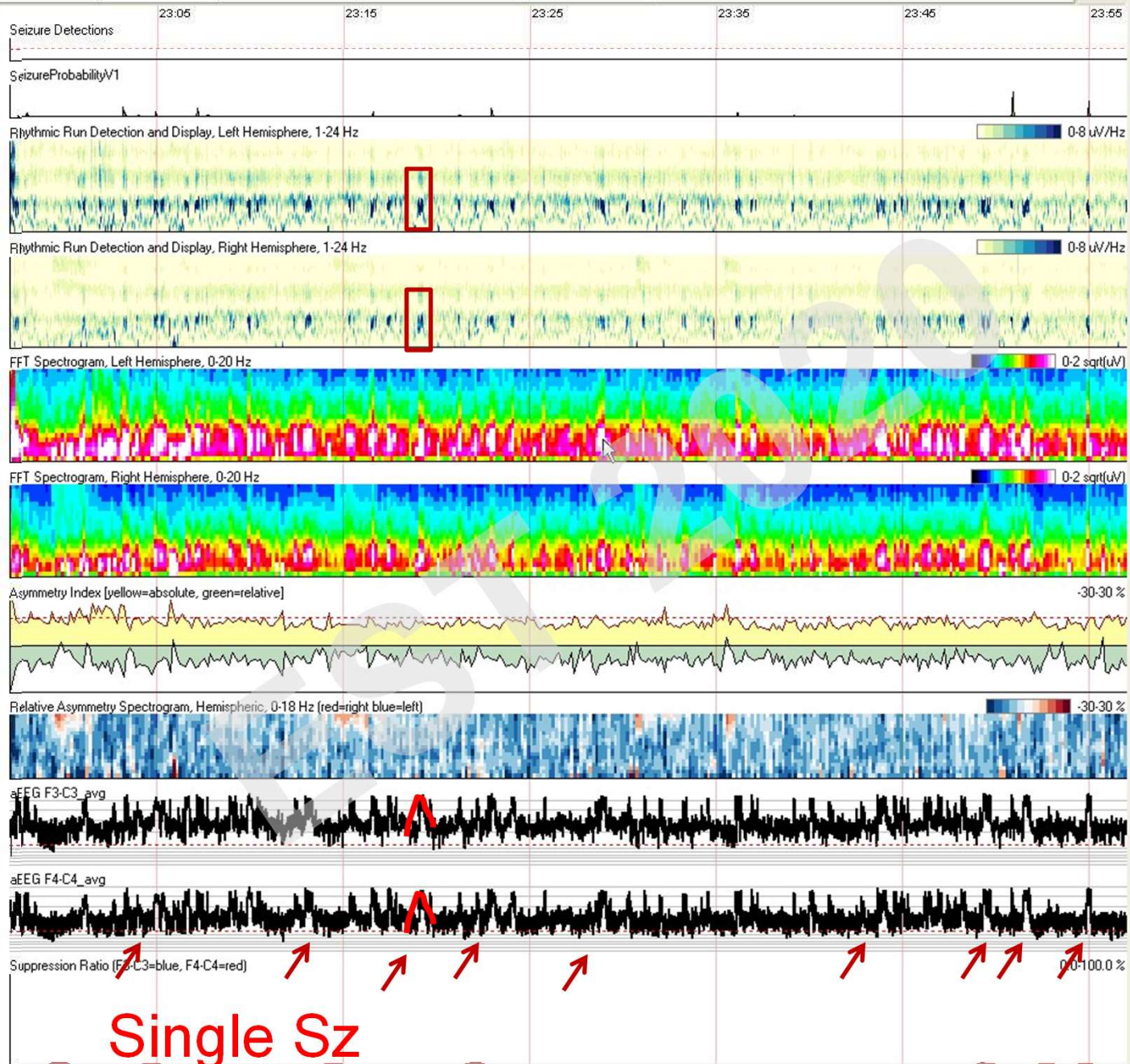
Comment List Bar

Time s G... Channel

Montage 10 uV 1 Hz 70 Hz 50 On

Spikes Bursts Bookmarks R

- Review EEG
- Stop Monitoring
- Patient Info
- Zoom
- Control
- AAR IS OFF
- Artifact Rejection
- GO TO REAL TIME
- Go to Real-time
- E-mail
- Training



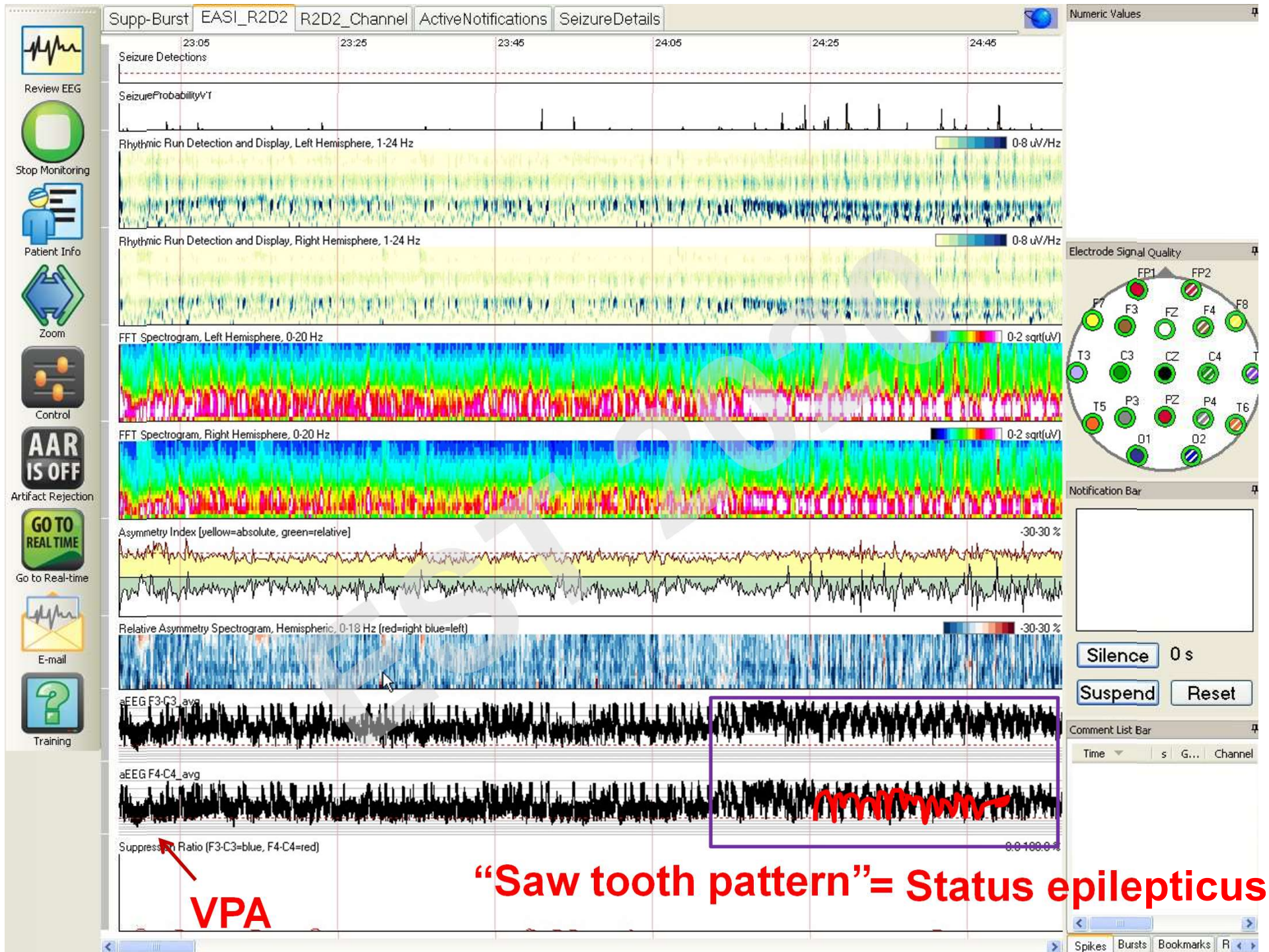
Notification Bar

Silence 0 s

Suspend Reset

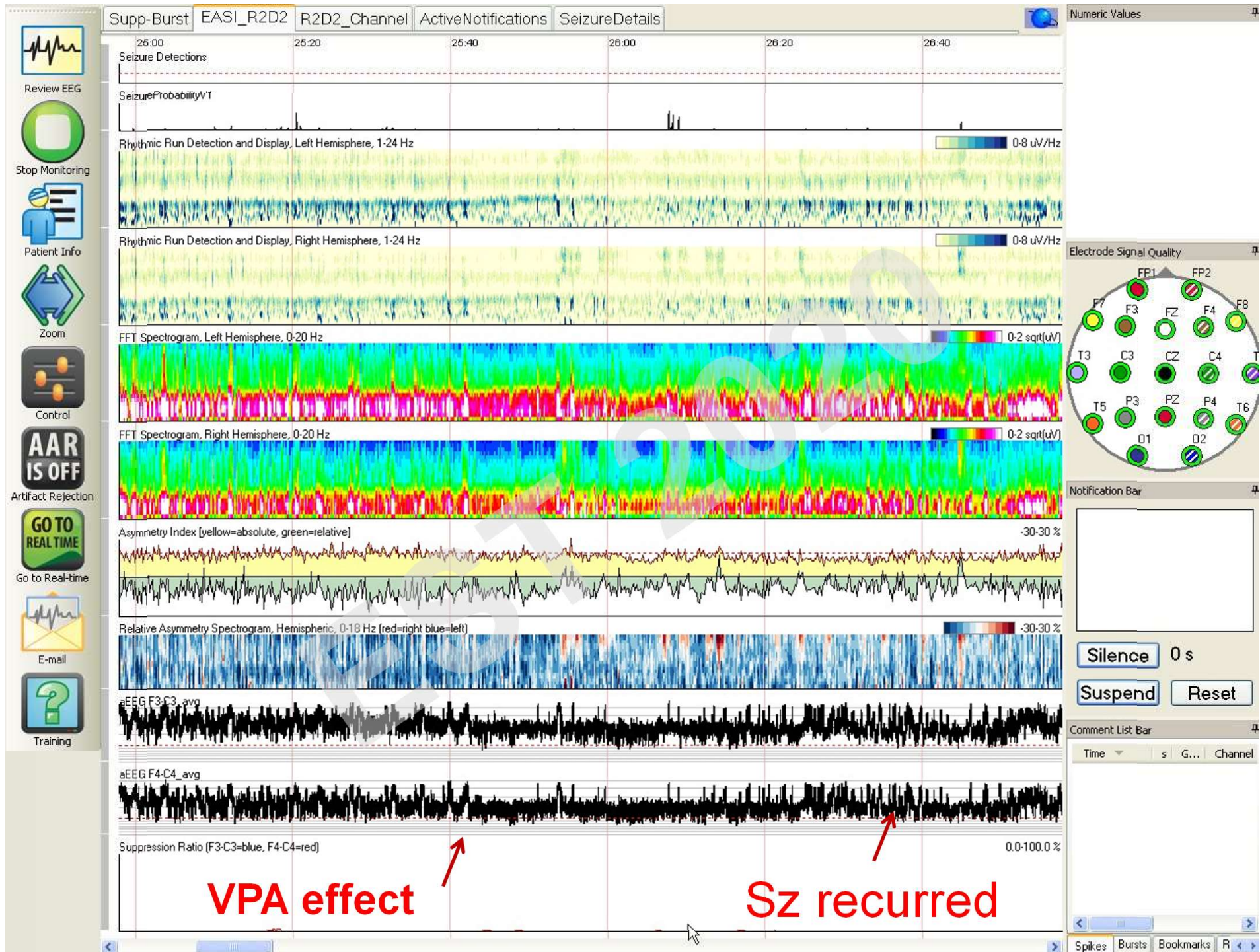
Comment List Bar

Time s G... Channel



VPA

“Saw tooth pattern” = Status epilepticus





Review EEG



Stop Monitoring



Patient Info



Zoom



Control



Artifact Rejection



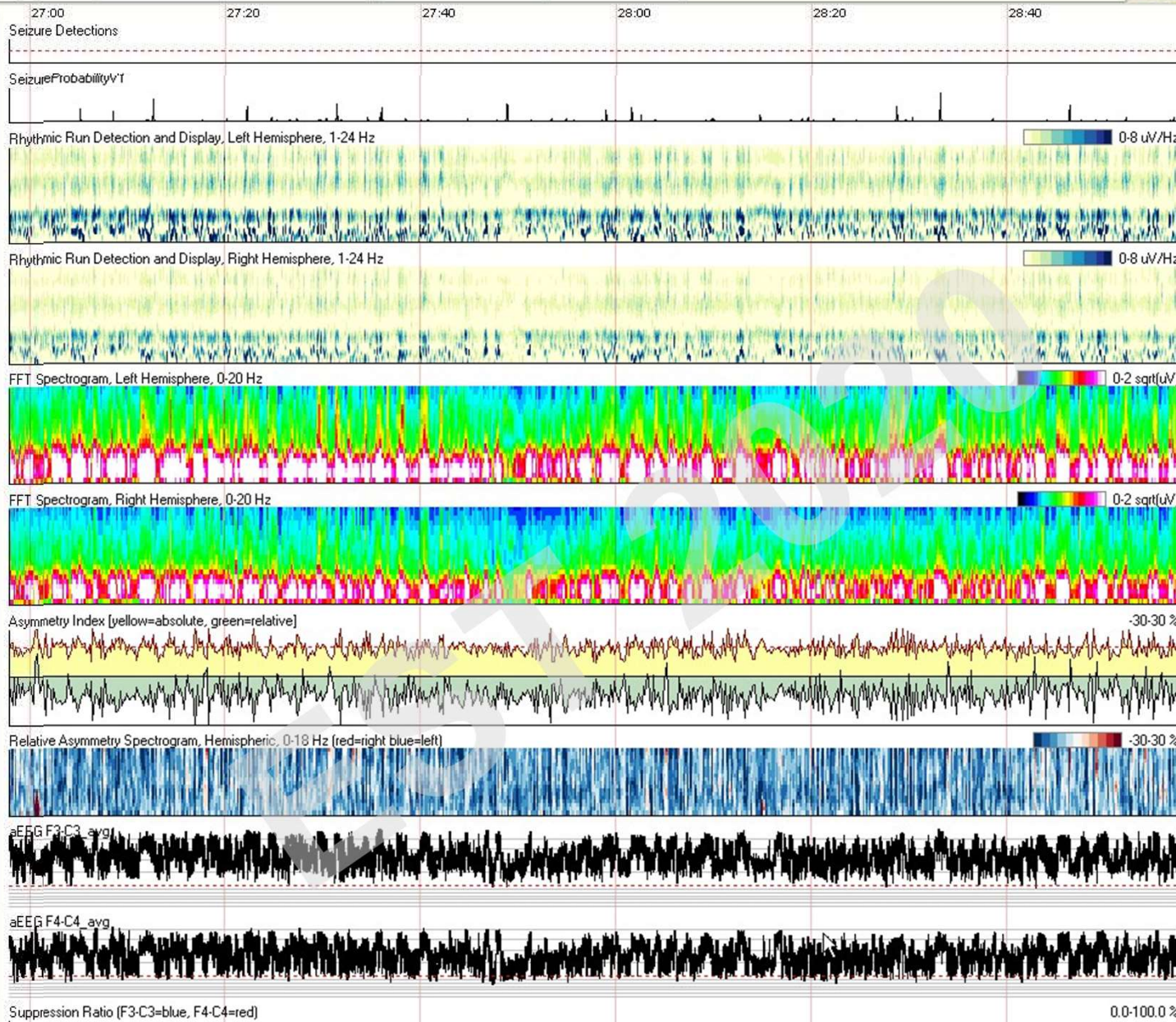
Go to Real-time



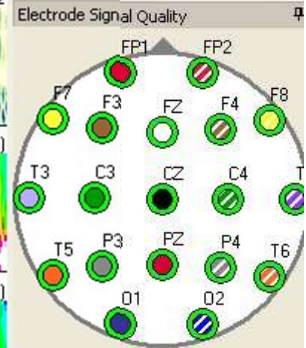
E-mail



Training



Status epilepticus



Notification Bar

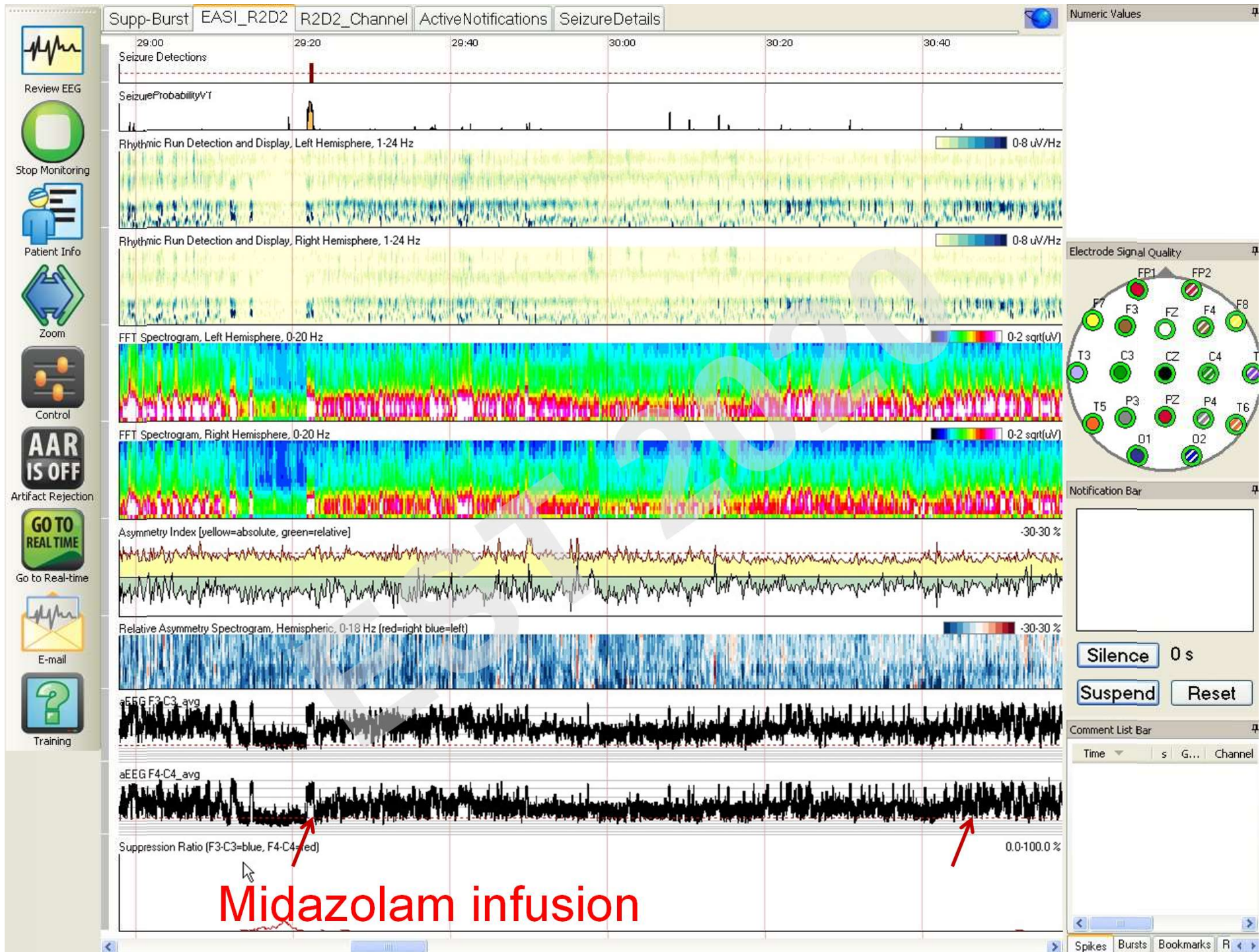


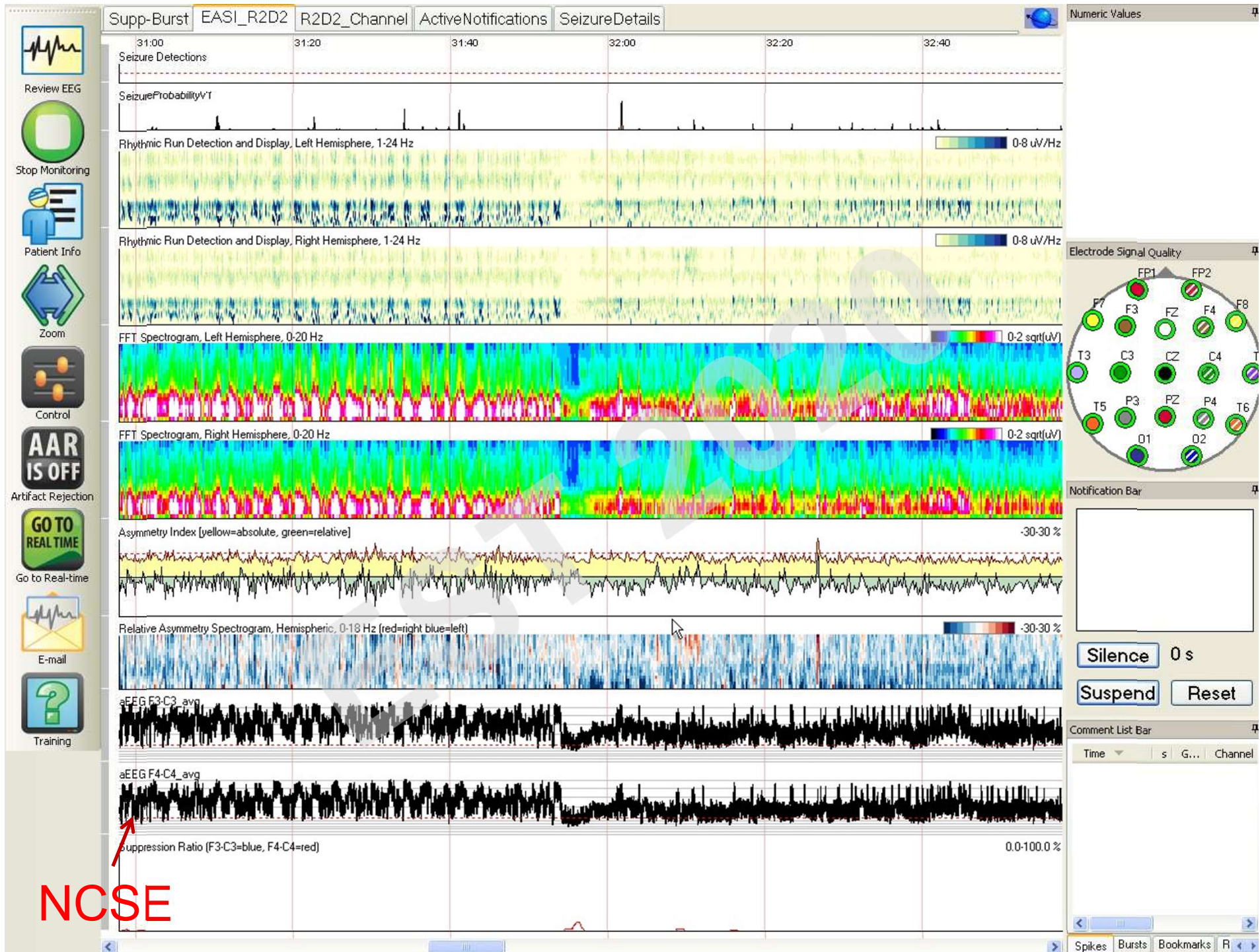
Silence 0 s
Suspend Reset

Comment List Bar

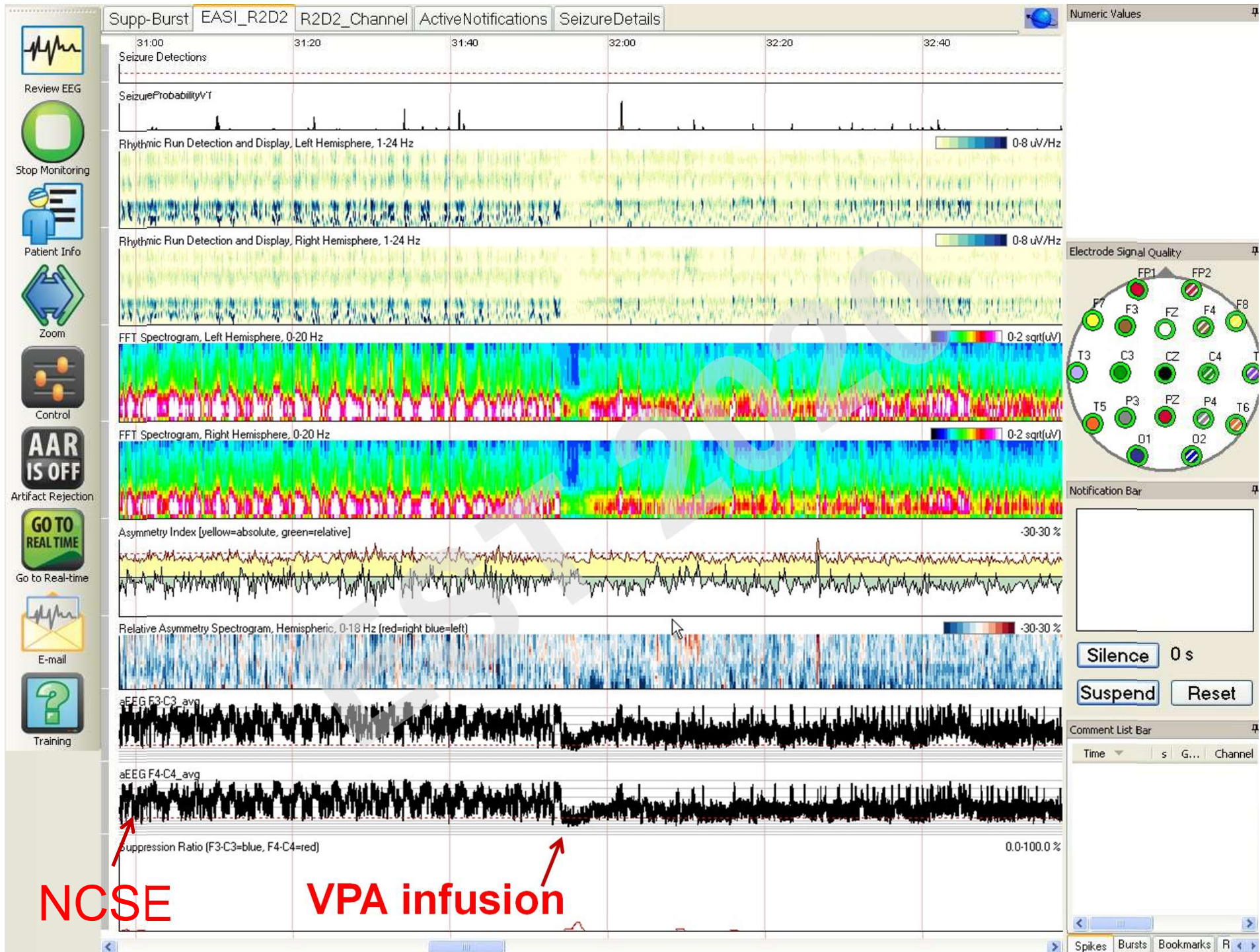
Time s G... Channel

Spikes Bursts Bookmarks R





NCSE



NCSE

VPA infusion

Review EEG

Stop Monitoring

Patient Info

Zoom

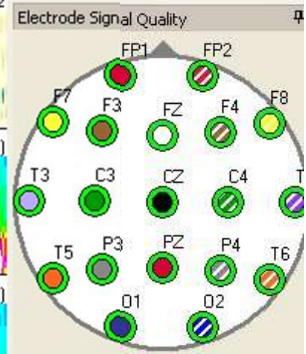
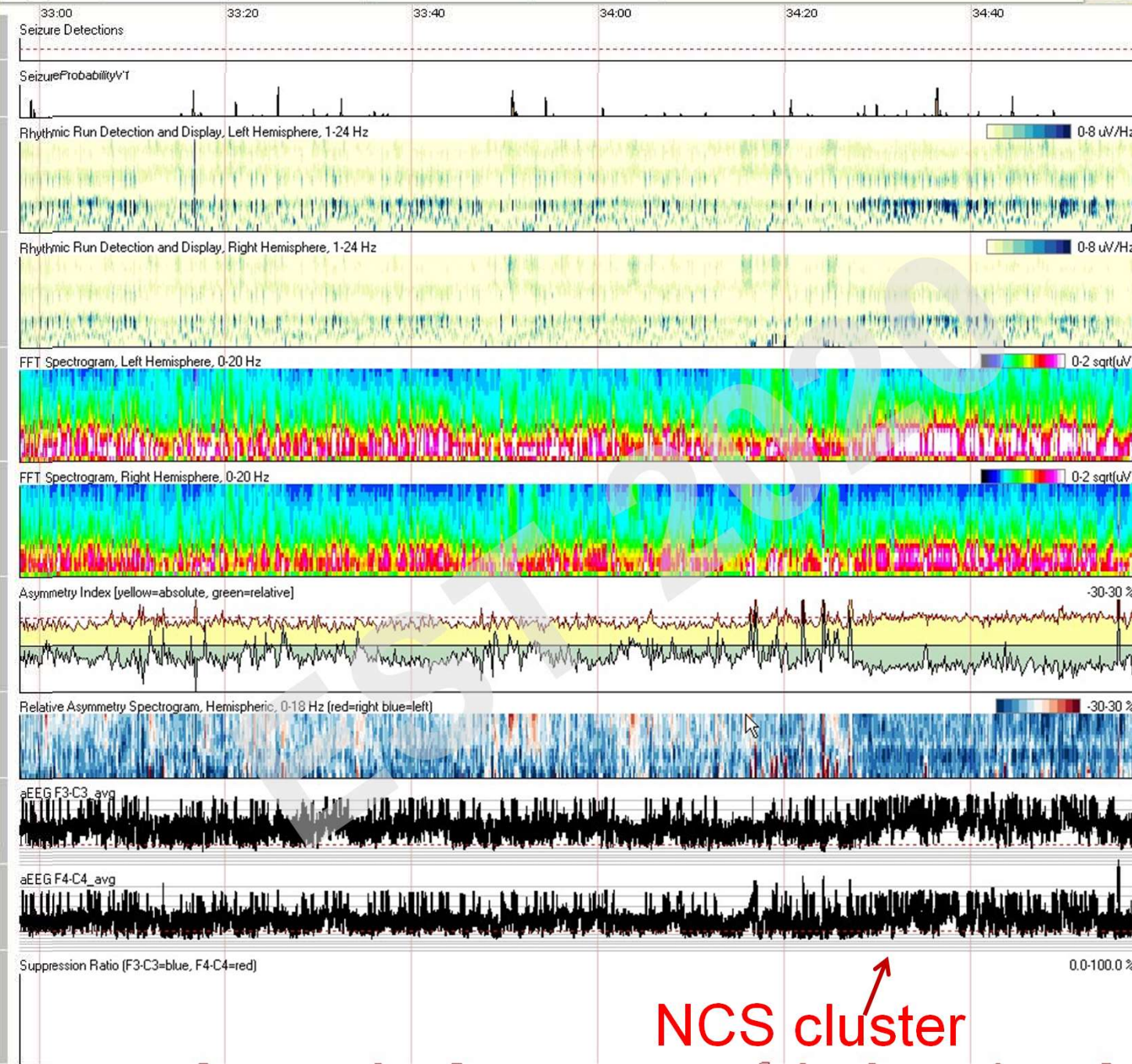
Control

AAR IS OFF
Artifact Rejection

GO TO REAL TIME
Go to Real-time

E-mail

Training



Notification Bar

Silence 0 s

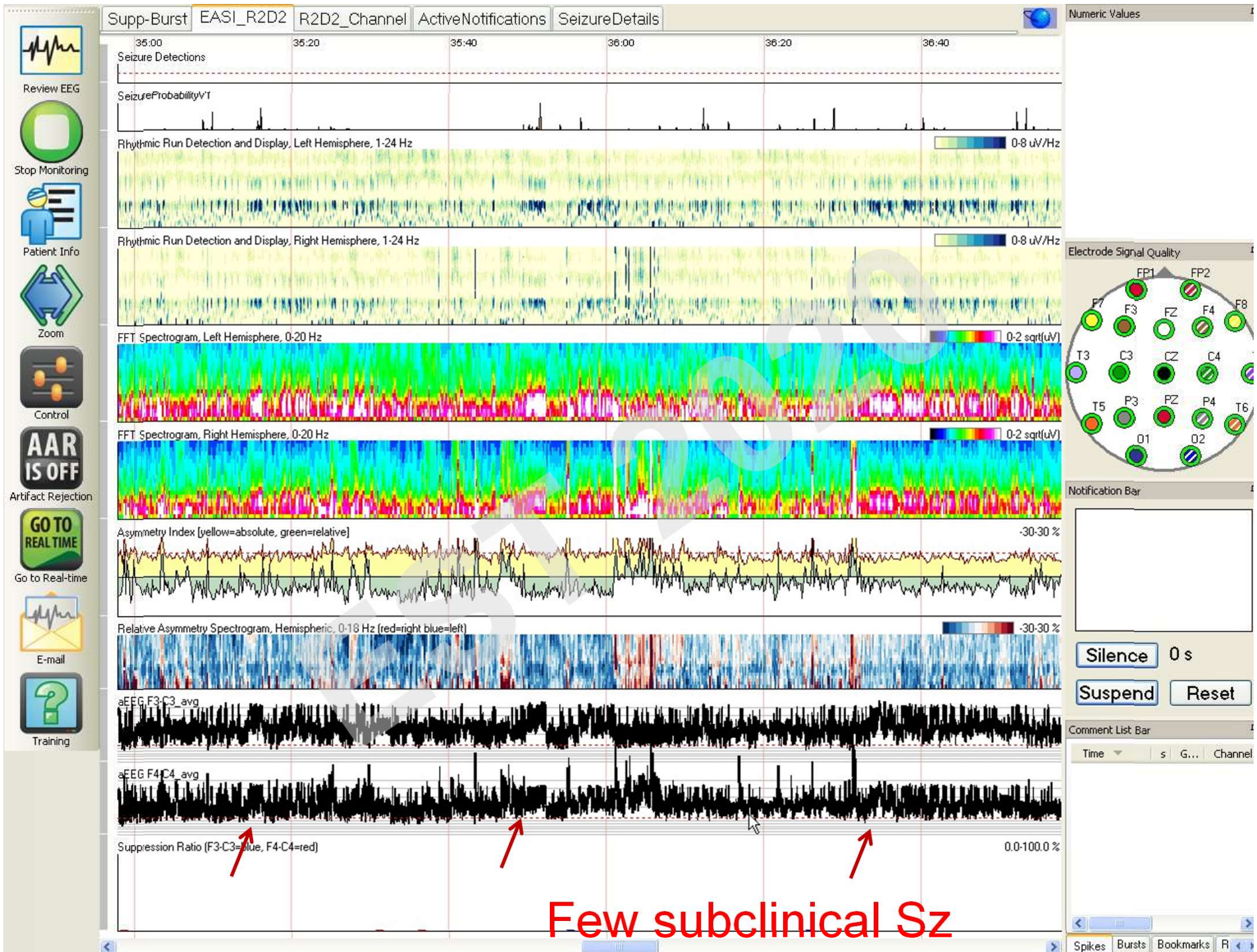
Suspend Reset

Comment List Bar

Time s G... Channel

NCS cluster

Spikes Bursts Bookmarks R



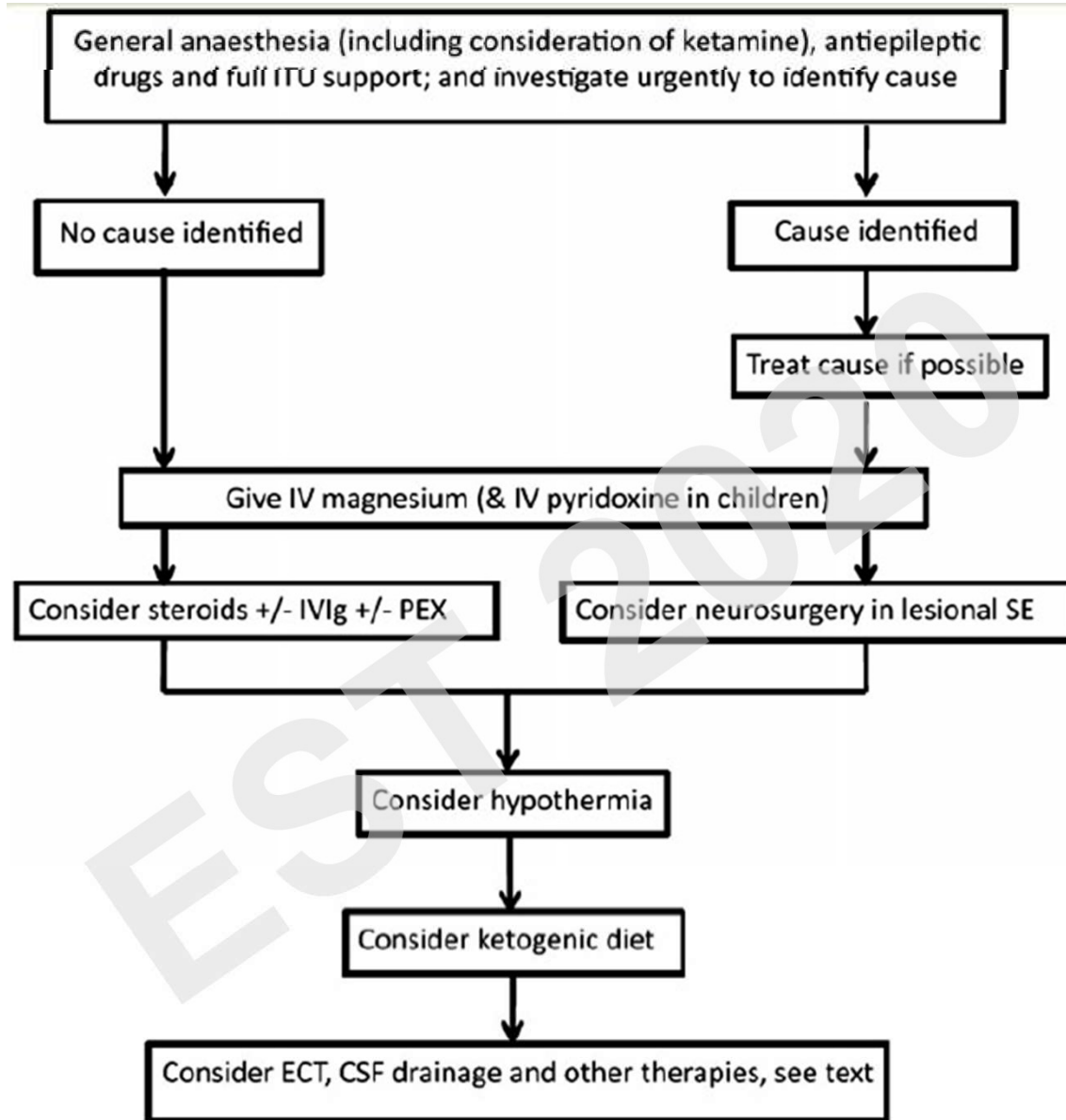
case

- weaning Midazolam after 48 h
 - Sz recur
 - AED added → still failed weaning
 - Superrefractory SE
- Parenteral Ketogenic induction
 - Off Midazolam & VPA infusion

super-refractory SE

status epilepticus that

- continues or recurs 24 h or more after the onset of anaesthetic therapy
- recurs on the reduction/withdrawal of anaesthesia



The treatment of super-refractory status epilepticus: a critical review of available therapies and a clinical treatment protocol. *Brain*. 2011;134(10):2802-2818

SRSE

- Any AED you can get
- Anesthetics(continuous infusion/ inhaled)
- ImmunoRx: Steroid/IVIg/Plasmapheresis
- Mg
- Ketogenic diet: enteral & parenteral
- Surgery
- Therapeutic hypothermia
- Neurostimulation: VNS/DBS/RNS/TMS/ECT

RSE/SRSE & Therapeutic hypothermia

- Anecdotal evidence from small case series
- systematic review- 62.5% Sz cessation (n=40)
- HYBERNATUS
 - multicentre, open-label RCT (n=270)
 - No significant difference in Glasgow outcome score at 90 days (43% VS 49%)

- Zeiler FA, Zeiler KJ, Teitelbaum J, Gillman LM, West M. Can J Neurol Sci 2015;42:221–9.

- Legriel S, Lemiale V, Schenck M, Chelly J, Laurent V, Daviaud F, et al. N Engl J Med 2016;375:2457–67.

RSE/SRSE & VNS

- Anecdotal evidence from small case series
- systematic review 2015 (n=28) 76% Sz cessation in generalized
 - 26% Sz cessation in focal
- systematic review 2019
 - 74% Sz cessation (n=38)

- Zeiler FA, Zeiler KJ, Teitelbaum J, Gillman LM, West M.. Epilepsy Res 2015;112:100–13.
- Dibul e-Adjei, Trinkka E et al. Brain Stimulation 2019; 1101-1110

RSE/SRSE & DBS/ TMS/ RNS

- DBS – a few case reports of RSE cessation from ATN, centromedian DBS
- TMS – systematic review (n=21)
 - 23.8% partial and 47.6% complete response
 - 73.3% recurrence
- RNS – 1 case report – adult with FCD, SRSE ceased in 15 d

- E. Trinka, F. Brigo . Epilepsy & Behavior 2019; 101:1-6
- Ernst L, et al. J Clin Neurophysiol 2019;36:242–5.
- Zeiler F, et al. Epilepsy Res Treat 2015:678074.

RSE/SRSE & ECT

- Anecdotal evidence from case reports and small case series
- systematic review (n=19)
 - 21.0% partial response
 - 36.8 % complete response

- E. Trinka, F. Brigo . Epilepsy & Behavior 2019; 101:1-6
- Zeiler Faet al. Seizure 2016;35:23–32.

Take-home

- qEEG – save time & allow quick response, but should be confirmed by raw EEG
- Automated seizure detection – sensitivity affected by many factors
- TH – no supporting evidence from recent RCT
- VNS/RNS/DBS/ECT – anecdotal evidence from systemic reviews of low level studies

Thank you
for your attention

EST 2020