ESETT EEG ANCILLARY STUDY

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Established Status Epilepticus Treatment Trial

Outline

- Significance/Purpose
- Study Overview
- Specific Aims
- Study Equipment
  - Jordan BraiNet
  - RhythmLink Disposable PressOn™ electrodes
- Study Approach
- Challenges
- Sample Set-up and EEG

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Significance/Purpose

- Emergent EEG (eEEG) would allow for early identification of SE
- Early treatment is key to avoiding pharmacoresistance
- A feasible system for eEEG in the ED could usher in a new standard of care for SE and help define a new era in SE treatment

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Ancillary EEG Study Overview

- Subset of ESETT patients
- Validate ESETT primary outcome:
  - Clinical cessation of seizures
  - Important patient-oriented outcome but how prevalent are misclassification errors?
- EEG is gold standard for determining seizure cessation
  - Is eEEG practical?
  - Should it be used for all urgent patients?

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- **AIM 1:** To characterize the operational parameters of obtaining an eEEG, applied by a non-EEG technologist, among patients with SE in the ED within sufficient time to evaluate immediate therapeutic outcomes.

  - This requires
    - Trained, available non-EEG techs
    - Foolproof technical setup
    - No interference with clinical care
    - Quick data quality check

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- **AIM 2:** To determine the inter-rater agreement for the presence or absence of electrographic SE, and the time of seizure cessation, from an eEEG collected within 60 minutes of enrollment in ESETT, using a rapid and quantitatively implementable scoring system on a cloud-based EEG platform.

- This requires
  - Consensus definition of SE
  - Quantifiable, reproducible
  - Assessable with statistics

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- **Aim 3:** To characterize the concordance of clinical and electrographic outcomes in ESETT participants and to qualitatively and quantitatively describe discordant clinical scenarios

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EEG Equipment/Set-up

- All equipment is FDA approved
- Jordan Neuroscience BraiNet®
  - Pediatric and adult sizes
  - Full international 10/20 system
    - 19 recording electrodes, ground and reference

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EEG Equipment/Set-up

- RhythmLink Disposable PressOn™ electrodes
  - Subdermal
  - Minimize infection risk

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Approach: Aim 1 Feasibility

- Study personnel
  - Will NOT have prior EEG experience
  - Standardized training: in person, video
- Study population
  - Inclusion
    - ESETT pt not at their baseline mental status
  - Exclusion
    - Returned to baseline mental status
    - Recent (6 months) skull defect
    - Extensive scalp infection/wound precluding electrode placement

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Approach: Aim 1

- Consent
  - Similar to ESETT patients will be unable to provide consent
  - Anticipate either
    - surrogate consent or
    - waiver of consent initially with delayed consent to use data

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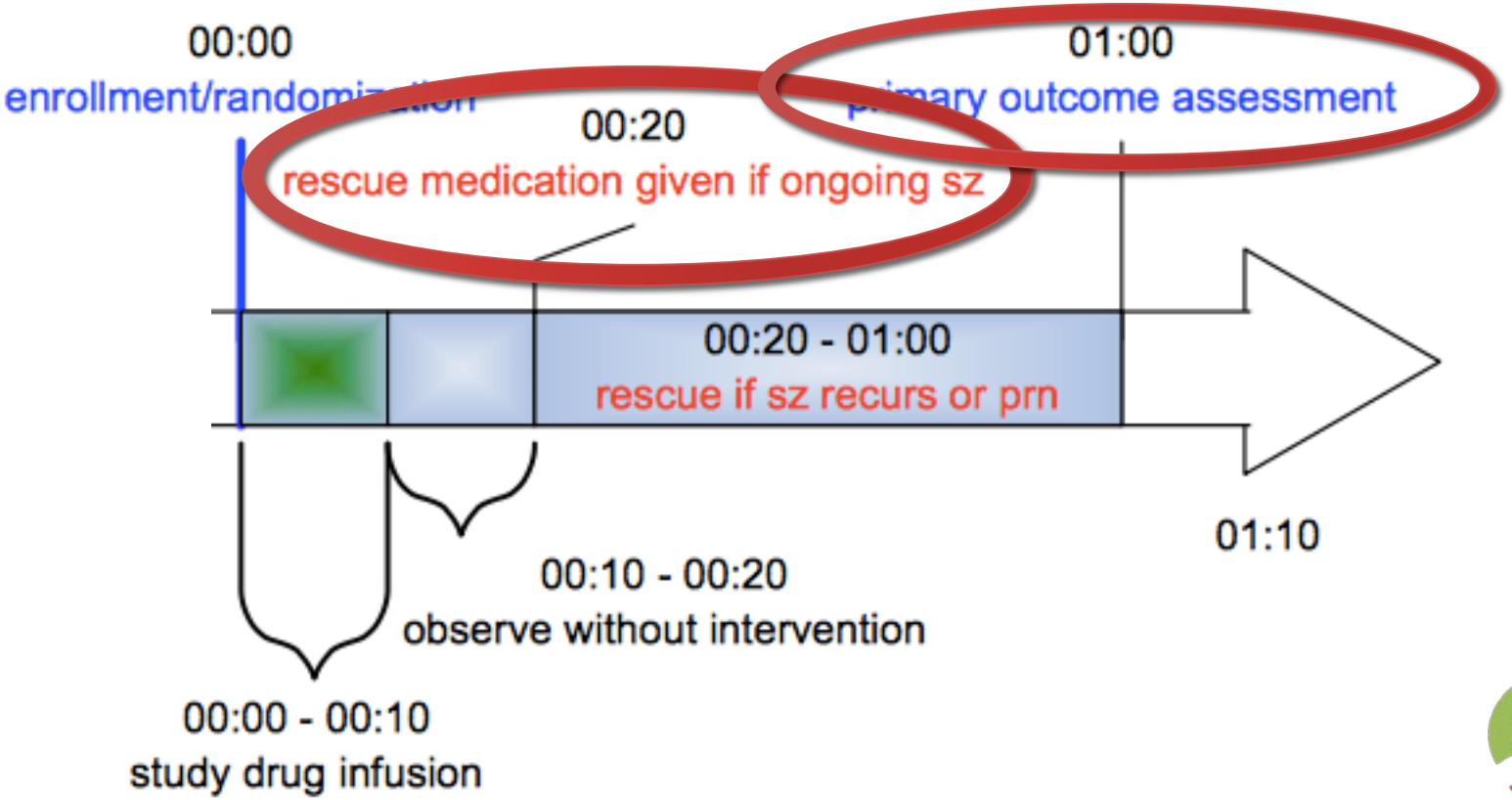
Approach: Aim 1

- Timing of EEG



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Approach: Aim 1

- Primary outcome: Feasibility
  - Time sensitive
    - Series of time points detailing EEG hookup process
  - Quality
    - # of electrodes dislodged
    - Signal to noise ratio of 3:1
    - Questionnaire for expert EEG reviewers
  - Interference with clinical care
    - Post-EEG questionnaire for primary nurse and physician
    - Was EEG disconnected early

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Approach: Aim 2 IRR

- EEGs will be reviewed at a later date
  - Panel of 3-5 “expert” reviewers
- IRR for EEG interpretation quite variable
- Proposed Likert Scale
  1. Definite SE on EEG
  2. Likely SE (would treat further)
  3. Likely not SE (would not treat further)
  4. Definitely not SE
  - Did the EEG improve over time?

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Approach: Aim 2

- Salzburg Consensus Criteria and ACNS
  - Patients without preexisting epileptic encephalopathy
    1. Epileptiform discharges (EDs) >2.5 Hz
    2. Spatiotemporal evolution of either
       a) EDs <2.5 Hz or
       b) Rhythmic activity (≤4 Hz)
    3. Subtle ictal clinical phenomena with
       a) EDs <2.5 Hz or
       b) Rhythmic activity (≤4 Hz)
    4. If 1-3 not fulfilled, would need to document electrographic response to AEDs

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Approach: Aim 3 Concordance

- Qualitatively and quantitatively describe the scenarios

ESETT \ EEG	No electrographic seizures	Electrographic Seizures	Total
Clinical SE cessation			
Ongoing SE			
Total			

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Challenges

- Aim 1
  - How many sites to involve
  - Who will be doing the EEGs at each site
  - Timing of EEG initiation
  - Assessing/determining return to baseline mental status as an exclusion criteria
  - Defining an interruption in standard clinical care
- Aim 2
  - Definition of electrographic seizure and SE
  - Not differentiating between seizures and SE electrographically
  - How to deal with patients with preexisting epileptic encephalopathy
  - How much can we rely on having clinical data for our definition of SE
  - Salzburg Consensus Criteria
    - "for research purposes, patient qualifies for NCSE if EEG and/or clinical improvement is documented, provided the clinical context is also in concordance with that"
- Aim 3
  - How valid is concordance if we are not studying the entire ESETT population

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Sample Set-up