Substudy Supplement

ELECTRO-BOOST: Electroencephalography for cerebral trauma recovery and oxygenation
An observational cohort study within BOOST-3 evaluating the relationship between established biomarkers of metabolic demand (PbtO2), EEG abnormalities (ESz and HFPD), clinical outcome, and treatment, seeking to identify dynamic EEG biomarkers of secondary injury that will enable future clinical trials seeking to improve functional outcomes for sTBI patients.

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1 Study Operations

ELECTRO-BOOST is an observational substudy that will evaluate a subset of patients in the parent BOOST-3 clinical trial, conducted within the Strategies to Innovate EmeRgENcy Care Clinical Trials Network (SIREN). The SIREN Clinical Coordinating Center at the University of Michigan will serve as the Clinical Coordinating Center for the ELECTRO-BOOST study. The SIREN Data Coordinating Center at the Medical University of South Carolina will serve as the Data Coordinating Center.

Approximately 15 BOOST-3 sites are expected to participate in ELECTRO-BOOST. It is expected that each participating site will enroll on average 6 BOOST-3 subjects per year in whom ELECTRO-BOOST data will be collected, allowing the ELECTRO-BOOST study to evaluate 200 patients within 5 years.

1.1 SIREN Organization

The NIH created SIREN to enable the conduct of high-quality, multi-site clinical trials to improve the outcomes for patients with neurologic, cardiac, respiratory, and hematologic, and trauma emergency events.

1.2 SIREN Clinical Coordinating Center (CCC)

The SIREN Clinical Coordinating Center (CCC) is located at the University of Michigan. The CCC will provide the following support for the study:

- integration with the network and the parent trial
- facilitation of regulatory compliance and CIRB and DSMB communications
- subcontracting to Hubs and spoke sites through BOOST-3 master agreements
- assisting with site training and communications
- monitoring of site performance

1.3 Data Coordinating Center (DCC)

The SIREN Data Coordinating Center (DCC) is located in the Data Coordination Unit housed within the Department of Public Health Sciences at the Medical University of South Carolina. The DCC will provide the following support for the study:

- Data Management: Development of Case Report Forms, data quality assurance, database technical support.
- Statistical: Input to and review of unblinded statistical analysis performed by the ELECTRO-BOOST Analytics Core, generation of enrollment and CRF completion reports, participation in writing of manuscripts, preparation of public use data set.
- IS/IT: Implementation of the required Case Report Forms in the existing BOOST CTMS, system infrastructure support.

1.4 EEG Core

The ELECTRO-BOOST EEG Core will work to label the EEG records. Members will:

- Apply standardized Critical Care EEG Monitoring Terminology to label and quantify EEG findings.
- Adjudicate findings to achieve consensus labels.
- Perform semi-automated label propagation using tools made available for the project (in collaboration with M. Westover, MGH).

1.5 Analytics Core

The ELECTRO-BOOST Analytics Core will work to apply biostatistical and engineering techniques to:

- Evaluate brain tissue oxygen, EEG label, and clinical data such as interventions and medications from CRF data to identify physiologic and clinical change points.
- Quantify the burden of EEG features, brain tissue hypoxia, clinical interventions, and outcomes, both through applied engineering and testing of commercially available tools.
- Test hypotheses of the project's specific aims assessing the associations between EEG activity, brain tissue hypoxia, clinical interventions, and outcomes.

Members include Drs. Gilmore, Kim, and Zavari (Yale), Rosenthal, Sharma, and Zabihi (MGH), Heldt (MIT), and others with interest as per the SIREN policy on secondary, tertiary, and quaternary publications.

1.6 Contact Information and Whom to Call

A. For immediate emergency assistance with ELECTRO-BOOST procedures, please use the 24/7 ELECTRO-BOOST Principal Investigator call schedule available here to find the number to call.

B. For immediate emergency assistance with general BOOST-3 study questions and concerns (enrollment, clinical, protocol, adverse events, etc.), please contact the 24/7 BOOST-3 PI Hotline at 855-4-BOOST3 (855-426-6783)

C. For other, non-urgent, questions, please refer to the roster below for whom to query by email.

1.7 ELECTRO-BOOST Staff Roster

Team Member	Role	Contact
Emily Gilmore, MD	Contact Principal Investigator, EEG Core, Analytics Core	Yale University Emily.gilmore@yale.edu
Eric Rosenthal, MD	Principal Investigator, EEG Core, Analytics Core	Massachusetts General Hospital erosenthal@mgh.harvard.edu
Kan Ding, MD	Principal Investigator, EEG Core, Analytics Core	UT Southwestern Medical Center Kan.ding@utsouthwestern.edu
Ramon Diaz-Arrasita, MD, PhD	Co-Investigator, EEG Core	University of Pennsylvania Ramon.diaz-arrastia@pennmedicine.upenn.edu
Robert Silbergleit, MD	Co-Investigator, CCC PI	University of Michigan
Valerie Stevenson, MS	Administrative Director	University of Michigan
Erin Bengelink, MA	Site Manager	University of Michigan
Sharon D. Yeatts, PhD	DCC PI	Medical University of South Carolina yeatts@musc.edu
Sara Butler	DCC DM	Medical University of South Carolina Butlers@musc.edu
Hitten Zavari, PhD	Analytics Core	Yale University
Jennifer Kim, MD	Analytics Core	Yale University
Morteza Zabihi, PhD	Analytics Core	Massachusetts General Hospital
Guneeti Sharma, MS	Analytics Core	Massachusetts General Hospital
Thomas Heldt, PhD	Analytics Core	Massachusetts General Hospital / Massachusetts Institute of Technology

2. BOOST-3 Protocol

The BOOST-3 protocol is publicly available. It can be viewed by anyone with the URL address, and the public can find the link from the SIREN and BOOST-3 websites.

Clarifications, interpretations, and elaborations of the BOOST-3 protocol are found in the BOOST-3 Manual of Procedures. Refer questions and comments about the protocol to the SIREN Clinical Coordinating Center. This ELECTRO-BOOST Manual of Procedures will describe procedures specific to centers collecting data as part of the ELECTRO-BOOST study.

3. Eligibility Criteria

I. Inclusion Criteria

- Randomized in BOOST-3 parent study at a participating ELECTRO-BOOST site.
- Undergoing continuous EEG monitoring +/- electrocorticography as part of routine clinical care (specifically a montage containing at least 14 scalp EEG electrodes, unless an ELECTRO-BOOST PI has approved otherwise) for a majority of the duration of intracranial monitoring recommended in the BOOST-3 MOP.

II. Exclusion Criteria

- Inability to undergo cEEG (extensive scalp burns, head lice, allergy)

III. BOOST-3 Inclusion and Exclusion Criteria

Refer to BOOST-3 protocol

4 Enrollment and Informed Consent

All patients who are eligible for the BOOST-3 study, who are enrolled at designated ELECTRO-BOOST sites, will also be evaluated for inclusion in the ELECTRO-BOOST analysis**.** The process of informed consent for BOOST-3 is detailed in the BOOST-3 MoP.

4.1 Consent Process

ELECTRO-BOOST does not require a separate consent process because this substudy does not introduce any new or additional interventions, risks, or assessments beyond those described in the parent trial and consent document. The substudy simply aggregates more granular detail of the same physiological and clinical data collected in the parent trial. Collection of these kinds of data is already described in the parent IRB approved protocol and consent document. Thus, an LAR will consent to collection of these data prospectively or to continued collection following an EFIC enrollment as per parent trial processes. Notification and consent to continued participation typically occurs prior to most ELECTRO-BOOST data collection.

Subjects or their LAR may withdraw consent from participation in BOOST-3 at any time. Discontinuing participation in BOOST-3 also discontinues participation in ELECTRO-BOOST. No further data will be collected or analyzed after the time of withdrawal of consent and discontinuation of participation.

4.2 Subject ID Assignment

Participants in ELECTRO-BOOST will be identified using only their BOOST-3 subject ID

5 Study Team, Site Activation and Clinical Team Training

In addition to the study team training plan listed in the BOOST-3 MoP section 5, the site study team will identify clinical personnel who will receive training in cEEG monitoring connectivity, eligibility criteria, and other clinical data collection and transfer.

The participation of a physician with experience in ICU EEG monitoring is required if the ELECTRO-BOOST site PI does not have this experience. Centers are selected for inclusion in ELECTRO-BOOST by their routine performance of continuous EEG after severe TBI and the clinical infrastructure of EEG technologists and clinical neurophysiologists that review data regularly with knowledge of ACNS Critical Care EEG terminology. The site PI and study coordinators should meet with EEG team to review the ELECTRO-BOOST Substudy Supplement and educate the EEG team on the recording requirements for EEG data collection that will be used in the ELECTRO-BOOST substudy supplement, including the research team's need to perform clock synchronization and recording of reference location and other data elements important for ELECTRO-BOOST.

5.1 Initial Training

Virtual Investigator Meeting

During the initial Virtual Investigator Meeting in collaboration with the CCC, the EEG Core will train the study teams (using a train-the-trainer paradigm) including the ELECTRO-BOOST site PI and clinical research coordinator.The ELECTRO-BOOST EEG Core will prepare training materials on substudy eligibility, collection of clinical data on timing and concurrent medications, connection and troubleshooting of the Moberg signal data aggregator, and transfer of EEG signal data. CCC and PIs will confirm sites' knowledge of how to designate patients for inclusion, general questions about procedures for performing follow-up assessments.

Local Site Training

The study teams will then train the clinical teams at their site. Training will be reinforced periodically throughout the study in a variety of formats, and will be available asynchronously on demand for refresher, remediation, or new study or clinical team members.

The EEG Core will provide reference tools to each site in the form of pocket cards, checklists, and documentation tools to assist in documenting clinical seizures and related intervention at the bedside. These tools will be available in the BOOST website's Toolbox. As the Toolbox will change over time, it's important to always go to the website to obtain the latest version.

All training materials will be posted on the BOOST website's Education and Training page.

Training as described in this Substudy Supplement will be disseminated to the PI, Study Coordinators, and key Clinical personnel. The site-PI will provide at least one or more in-service sessions to educate hospital physicians, nurses and other key personnel about the study, using resources provided by the EEG Core coordinators.

EEG Setup Training
The EEG Core PIs and coordinators will meet with individual sites to review progress regarding EEG monitoring technical setup, including:

- A plan for EEG setup and synchronization procedures
- Question about the ELECTRO-BOOST EEG Setup video
- Involvement of the local clinical neurophysiology team reviewing daily EEG and working with the clinical research coordinator to complete the EEG CRF worksheet
- Involvement of EEG technologists and/or coordinators performing splitting or jumping of EEG signals to enable synchronized Moberg and non-Moberg EEG recordings
- Plan to clinically read EEG while maintaining the study Moberg CNS Monitor off network as per the BOOST-3 MOP.

Training videos, slides, and webinars will be posted on the BOOST-3

5.2 Ongoing Training

The CCC, in coordination with the ELECTRO-BOOST PIs and EEG Core, will provide reinforcement training to ensure adherence to the Substudy Supplement; this is essential for the success of this study.

Specifically, following enrollment of a site's first BOOST-3 subject included in ELECTRO-BOOST, the site will be contacted for a debriefing on the subject's EEG monitoring. This training team, composed of the EEG Core and CCC staff, will document questions raised by the Study Team or key clinical personnel in a Frequently Asked Question (FAQ) log.

Additionally, at periodic Clinical Site Meetings, coordinators and investigators will present questions raised by enrollments among all ELECTRO-BOOST sites. Relevant new questions can be added to the FAQs page on the study website. These teleconferences will be recorded and posted on the study website's Education and Training page. Any additional study-related issues that require guidance will be documented in the FAQs log as an item for future discussion in teleconferences and/or future training presentations.

5.3 Retraining

Consistent with SIREN standard operating procedures, sites are required to retrain every 6 months if they do not submit ELECTRO-BOOST data for 6 months (notification takes place at 5 months), or if the sites are deviating from the Substudy Supplement, due to incomplete data collection or failure to collect uncorrupted EEG data. Retraining will be overseen by the ELECTRO-BOOST PIs, EEG Core coordinators team, and/or CCC and will assure that study team staff and applicable personnel are all familiar with the ELECTRO-BOOST Substudy Supplement.

Retraining will include:

1. Clinical team training.

2. Review of Data Training video or slides by team member as appropriate to their role.

The PI will sign the PI Attestation ELECTRO-BOOST Re-Training document once the study team has met all the re-training requirements. The attestation will be uploaded to the BOOST Database/WebDCU™.

5.4 Clinical Team Newsletter

ELECTRO-BOOST progress including subject accrual, new sites, recent FAQs, and amendments to the ELECTRO-BOOST Substudy Supplement will be included in BOOST-3 Newsletter. The newsletter will be posted on the BOOST-3 study website under the Newsletters tab.

5.5 Training Resources

Training resources will be prepared by the training team, CCC and DCC personnel and provided to sites at the time of their initial training period. All resources will be posted in the BOOST-3 website's Toolbox.

Resources may include:

Slide and/or Webinar Presentations
Videos (investigator meeting, instructional, important reminders, EEG setup, etc.)
Pocket Reference Cards (troubleshooting tips for EEG setup, the use of split/jump cable, and transmission of EEG data)

5.6 Substudy Supplement Amendment Dissemination

Substudy Supplement amendment updates will be presented to the study team in online training presentations, emails, newsletters, study website, and network steering committee and study coordinator meetings.

6 EEG Monitoring and Data Collection

6.1 EEG setup

Each site will use its own preferred clinical EEG setup and acquisition system for EEG recording. The EEG will be monitored and reviewed per institutional clinical continuous EEG protocols. An EEG Setup CRF will be completed on the day of set up and for subsequent days of EEG recording on which there are changes to the set up.

6.1.1 Systems and synchronization: The system/s used for the research EEG recording will be recorded on the CRF. At some centers, it will be possible to record EEG using the Moberg CNS monitor and another EEG system.

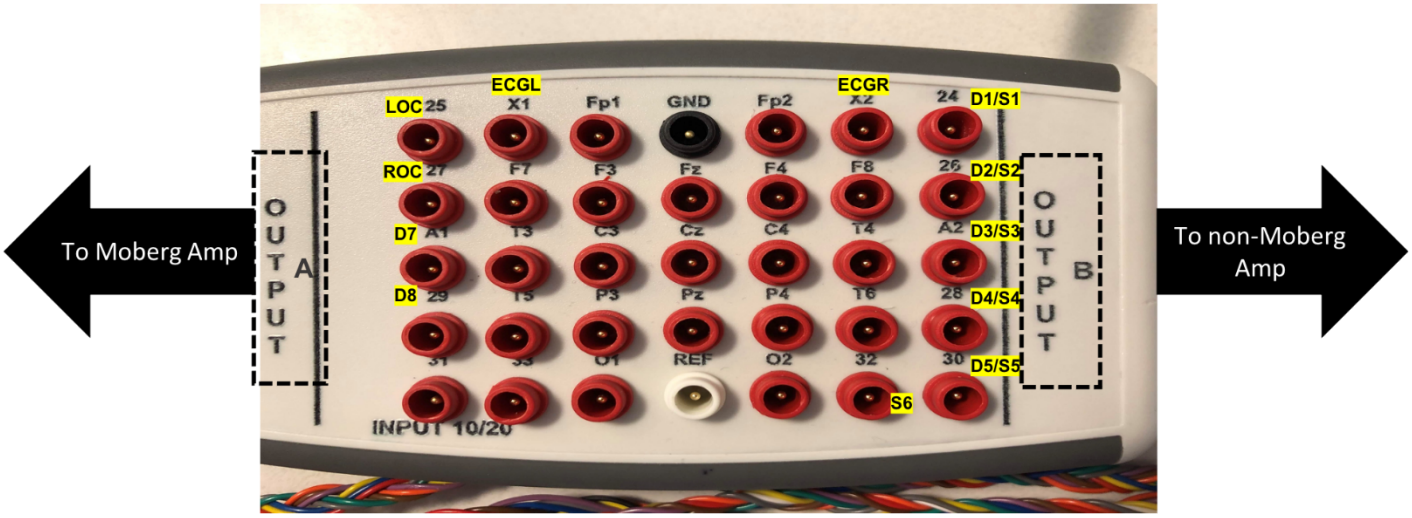
If a system other than the BOOST-3 Moberg CNS Monitor is used to record the research EEG, that system must be time-synchronized with the BOOST-3 Moberg CNS monitor in order for the aaims of the study to be investigated.

This synchronization will occur by:

A. Setting the time clocks on the Moberg CNS monitor and any additional EEG system to a network clock on the initial day of recording, and additionally after any system is rebooted. This synchronization, and the time is occurs, will be recorded on the EEG Setup CRF.

B. Sharing the EEG channels between the BOOST-3 Research Moberg CNS monitor and the other clinical EEG acquisition system using one of two methods:
    1. Connecting the patient's electrodes to a splitter box (Figure 1) from which the EEG electrodes are split to A) the BOOST-3 Research Moberg system and B) the clinical EEG acquisition system, or
    2. Connecting the patient's electrodes to the Moberg amplifier and using Jumper cables to connect each channel from the BOOST-3 Research Moberg system to the clinical EEG acquisition system.

Figure 1.



6.1.2. EEG Channels recorded

Reference channel recorded: The EEG setup CRF captures the location of the reference electrode for the scalp EEG and for the intracranial electrodes. These should be the same unless there is a patient-specific requirement that they are different, in which case the scalp reference should be split/jumped between the Moberg and non-Moberg amplifiers.

Scalp electrodes recorded:
In most cases, a full montage (19-21 channels) of scalp electrodes will be what the site obtains for clinical purposes. However, it is recognized that following a craniotomy, bandages or wounds may require a channel to be moved (preferred) or left off the scalp not recording (not preferred). In either setting, routine clinical care should involve the bandages being removed at the earliest time point to enable as complete a set of electrodes as possible to be placed as soon as possible. When subjects are not expected to have at least 14 channels of scalp EEG , these subjects should not be included in the ELECTRO-BOOST substudy without prior case-by-case approval by the ELECTRO-BOOST PI If a small number of electrodes must be left off the scalp, the EEG setup CRF will capture, daily, which channels were or were not recorded, in order to ensure the analyses are performed appropriately.. The CRF groups together those channels that are synonymous (e,g., T5/P7) as well as those that are functionally similar (e.g., FT9/T1).

For patients with intracranial recordings, splitting or jumping the reference channels requires particular attention. Because the Moberg EEG amplifier has a separate reference for intracranial

and scalp electrodes, we are requiring that centers use the distributed ELECTRO-BOOST EEG software protocol in which the Moberg scalp and auxiliary reference are "shared;" accordingly a jumper cable must connect the following channels on the Moberg EEG amplifier itself when intracranial recordings are performed: a) Moberg EEG amplifier scalp reference and b) Moberg EEG amplifier auxiliary reference.

Intraparenchymal depth electrodes recorded:
Based on the local clinical guideline, some patients may undergo placement of an intraparenchymal depth electrode. For these subjects, the location of this electrode should be captured on the EEG setup CRF, specifically left or right frontal, which will clarify its position with relation to the brain tissue oxygenation monitor.

Subdural strip electrodes recorded:
Based on the local clinical guideline at each institution, some patients may undergo placement of a subdural strip electrode on the cortical surface. For these patients, the location of this electrode should be captured on the EEG setup CRF, specifically left frontal, right frontal, left temporal, right temporal, or other, which will clarify its position with relation to the brain tissue oxygenation monitor.

6.2 Site-Level Local EEG Data Review
Analysis of continuous EEG data will be an important primary analysis of ELECTRO-BOOST study. Investigators at the clinical sites should work with the local neurophysiologist to ensure that EEG data is clean and free of artifacts. Periods when such data is artifactual as a consequence of the patient being disconnected from the monitors for transport to an imaging study or other procedure should be captured on the EEG Interruption Log CRF, and if possible should be annotated on the EEG recording itself. Times when the continuous data is uninterpretable due to artifact, equipment malfunction or other technical issue should also be documented in this manner. Research coordinators should review the clinical chart and query bedside nurses to confirm times when the patient was disconnected and identify the times during which there was disconnection or artifact on either the Moberg EEG, the other EEG system, or both.

The EEG Findings worksheet will be completed daily by the study team in collaboration with the neurophysiologist/epileptologist who is reading the clinical EEG as part of routine care for the patient each day. The site is responsible for interpreting and documenting findings on the EEG (inclusive of scalp and intracranial data). This will enable a check of central reading with the site to generate a consensus report, will clarify whether medical interventions were informed by the findings reported in real time, and will ensure that clinical events meeting electroclinical criteria for seizure based on video data are known to the central readers, who may otherwise misclassify them when reviewing EEG data without video.

6.3 EEG Data Transfer
At the end of the monitoring period, after the continuous EEG data is fully cleaned and annotated, bata collected both using the Moberg CNS monitor and any additional EEG monitoring system should be uploaded to the secure web server provided, as noted in the BOOST-3 Toolkit under Moberg Data Upload.

6.4 Concomitant Medication Log
In order to complete the aim of this study examining whether medications influence EEG activity or

clinical trends in recovery, the site will capture concomitant medications and time stamps given on the days of EEG monitoring. Dosing information for four classes of medications will be recorded in the Concomitant Medication Log:

- Oral and IV Anti-Seizure Meds:
  levetiracetam, fosphenytoin, phenytoin, lacosamide, valproic acid, brivaracetam, pregabalin, gabapentin, clobazam, clonazepam, diazepam, lorazepam, lamotrigine, perampanel, felbamate, oxcarbazepine, carbamazepine, topiramate, vigabatrin, zonisamide, cannabidiol
- IV Opioids/Sedative Medications:
  morphine, fentanyl, hydromorphone, dexmedetomidine
- IV Anesthetic Medications:
  midazolam, lorazepam, diazepam, phenobarbital, ketamine, propofol, pentobarbital
- IV Vasoactive Medications:
  phenylephrine, norepinephrine, dopamine, milrinone, dobutamine, epinephrine, nicardipine, clevidipine, labetalol, hydralazine, metoprolol, esmolol

If these medications can additionally be collected via electronic capture, the data may be uploaded securely to the EEG data portal, denoting labels for each column of information. On the first occasion of performing any uploads, the study leadership will be available for education.

6.5 Full Outline of Unresponsiveness (FOUR) Score (FOUR) Report

The FOUR score is a standardized neurological exam optimized for use in individuals with severely impaired consciousness. The FOUR score will be assessed and recorded on the CRF for 1) each calendar day while on EEG recording and 2) on the day of discharge or Day 14, whichever comes first, after randomization. A description of how to perform this instrument is located in the BOOST-3 Toolkit.

When and if possible, participants should be scored during periods when sedation is held. Consensus scoring in the presence of the patient's nurse and/or providers will enhance reliability.

6.6 Glasgow Coma Scale (GCS) Trend Report

The best GCS score is assessed daily as part of data collection for BOOST-3. However, ELECTRO-BOOST seeks to answer the question of whether GCS trend is associated with either quantitative EEG trends or medications. As such, the local site CRC will record all reliable GCS scores that are clinically performed and recorded in the electronic health record flowsheet data, including those documented by the bedside nurse.

7 Subject Tracking and Follow Up

Participants will be followed by study staff daily while hospitalized in the ICU through Day 14 if still admitted to the current hospital or prior to discharge if discharge occurs before Day 14. For details regarding post-discharge subject tracking and follow up refer to BOOST-3 MoP. Follow-up for ELECTRO-BOOST includes a CRF Medication Checklist, recording the subject's anti-seizure medications at discharge and day 180, at the scheduled BOOST-3 follow up visit.

8 Adverse Event Reporting and Safety Monitoring Plan

ELECTRO-BOOST is an observational study of data already acquired for clinical purposes using approved, commercially available diagnostic monitoring. The only incremental risk anticipated in ELECTRO-BOOST is exposure to an inadvertent breach of confidentiality. Significant breaches of confidentiality without injury will be reported as Unanticipated Problems Involving Risks to Participants or Others. Harm or interventions to prevent harm resulting from breaches of confidentiality will be reported as adverse events. Any breach of confidentiality will be reported in WebDCU as per the BOOST-3 MoP, and assessed in a manner consistent with existing BOOST-3 safety monitoring and other procedures including Independent Medical Safety Monitor review of all serious adverse events. Any event resulting specifically from ELECTRO-BOOST participation will be reviewed by the ELECTRO-BOOST leadership team. Adverse events reported in relation to the BOOST-3 trial do not need to be separately reported to ELECTRO-BOOST.

The SIREN DSMB oversight of ELECTRO-BOOST is encompassed by its oversight of BOOST-3.

9 Site Regulatory and Study Team Management

9.1 Regulatory Binder and Parameters Document

As the ancillary study of BOOST-3, no separate regulatory binder is needed for ELECTRO-BOOST. The regulatory binder and parameters documents for BOOST-3 are defined in detail in BOOST-3 MoP and the BOOST Regulatory Parameters Document .

9.2 Study Team Management

Site teams are managed within WebDCU's BOOST-3 database. Please refer to the BOOST-3 user manual on how to add/remove team members from the eDOA log, or update training certificates and documents.

Refer Section 5 of the Substudy Supplement for Clinical Team Training and BOOST-3 MoP section 5 for general training. Adequate training is required by the principals of the International Conference on Harmonization (ICH), Guideline for Good Clinical Practice (GCP).

9.3 BOOST-3 Site Readiness and Start-Up

BOOST-3 site readiness is confirmed by the BOOST-3 CCC separately and all BOOST-3 regulatory and training certifications are required to be uploaded in the BOOST-3 database. The SIREN-CCC will routinely monitor the database for regulatory compliance.

9.4 ELECTRO-BOOST Site Readiness

The ELECTRO-BOOST readiness checklist, developed by the ELECTRO-BOOST PIs, EEG Core coordinators, CCC and DCC staff, will be given to each site PI and primary study coordinator. The site will be scheduled for a readiness call.

This checklist should be completed prior to the time of the readiness call. The checklist will ask the study team to describe their processes addressing important aspects of the ELECTRO-BOOST study, cEEG setup including collection of EEG data on the Moberg and/or alternate EEG acquisition device with appropriate synchronization, and data collection and transfer, and patient follow up. From the BOOST-3/ELECTRO-BOOST team, one of the study PIs, EEG Core

coordinators, CCC and DCC staff will all participate in the readiness call.

During the call, site team members as well as ELECTRO-BOOST study leadership, site manager, and study project manager will discuss site training and ELECTRO-BOOST procedures. Any items needing further action as discussed during the call will need to be resolved/reconciled before each site can be activated.

Overview of ELECTRO-BOOST site readiness checklist for each ELECTRO-BOOST site will include:

- ☐ BOOST-3 regulatory compliance complete in WebDCU.
- ☐ Technology for EEG recording
- ☐ Technology for synchronization
- ☐ Training in EEG monitoring synchronization (jumper cables or splitter boxes)
- ☐ Verification of Moberg software protocol collecting EEG data or alternative system
- ☐ Verification of EEG montages utilized
- ☐ Verification of references including intracranial references utilized
- ☐ PI attestation and signed/dated Substudy Supplement uploaded to WebDCU

After successful completion of the readiness call, the site will be activated as an ELECTRO-BOOST site. A formal email informing the site and ELECTRO-BOOST teams will be sent when a site is 'released to collect ELECTRO-BOOST data.' **This email will serve as the formal communication for ELECTRO-BOOST site readiness.**

10 Site Monitoring

10.1 Site monitoring will be conducted through the BOOST-3 site monitoring mechanism.

10.2 EEG data quality and other items specific to ELECTRO-BOOST will be reviewed for completion and data quality by the ELECTRO-BOOST study team.

11 Reports

Reports can be generated from the BOOST-3 WebDCU system to generate a list of patients enrolled and data collected for the ELECTRO-BOOST ancillary study, as well as pending queries. Refer to BOOST-3 MoP section 13.

12 Retention of Study Records

Study records will be retained according to the BOOST-3 MoP.

13 Payment to Clinical Sites

Start-up payments:
No start-up payment available for this study.

Per-subject payment:
Per-subject payments are listed in the ELECTRO-BOOST milestone document as posted on the ELECTRO-BOOST website. These tiered payments are based on the activities included in the Substudy Supplement. Payments for each enrollment will occur in milestones related to EEG data quality check, CRF completion including medication data, and query completion.

All data related to the study visit must be submitted, undergo a quality check and be free of query prior to the full payment.

The per-enrollment Total Site Reimbursement is $2750, **inclusive of F&A**

14 Case Report Forms Study Book

14.1 CRF Study Book

The CRF study book is maintained in project documents under the Toolbox tab in WebDCU.

14.2 CRF Completion Guideline

Click here for the link to the CRF Completion Guidelines.

15 Publications and Data Sharing Policies and Procedures (link to SOP)

Please refer to the SIREN SOP.

16 ELECTRO-BOOST Frequently Asked Questions

FAQs will be listed on the ELECTRO-BOOST website. New Q&A will posted and this page will be regularly updated.