

Research Protocol Template

Any research related activity involving human subjects must be approved by the REC prior to initiation. The following template is meant to serve as a guide to assist investigators in developing a protocol for REC review. Please note that not all sections of this template will apply to all studies.

Study Name:

BI-SENSES: Validation of nasal versus frontal (forehead) placement of the SedLine® sensor through processed electroencephalography in adult patients undergoing general anesthesia.
A Prospective cohort study

Principal Investigator(s): Boris Tufegdzcic, MD

Principal Investigator Mentor (if applicable): N/A

Institute(s): Anesthesiology Institute

Protocol Version: 1.0

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Summary of Changes from Previous Version (if applicable):

Affected Section(s)	Summary of Revisions Made	Rationale

Investigator Signature Page

Protocol Version: 01

Protocol Date: 15.03.2019.

Study Name

BI-SENSES: Validation of nasal versus frontal (forehead) placement of the SedLine® sensor through processed electroencephalography in adult patients undergoing general anesthesia. A Prospective cohort study

Coauthors:

1. Dr Andrey Khozenko, Anaesthesiologist, Anaesthesiology Institute, Cleveland Clinic Abu Dhabi
2. Vinay Byrappa, Anaesthesiologist, Anaesthesiology Institute, Cleveland Clinic Abu Dhabi
3. Aliaksandr Ruzhyla, Anaesthesiologist, Anaesthesiology Institute, Cleveland Clinic Abu Dhabi
4. Massimo Lamperti, Anaesthesiologist, Anaesthesiology Institute, Cleveland Clinic Abu Dhabi

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable federal regulations and ICH guidelines.

Principle Investigator: **Boris Tufegdzic, MD**

Signed:

A handwritten signature in black ink, appearing to read 'B. Tufegdzic', written over a horizontal line.

Date:

20 03 2019.

Name and Address of Institution:

Cleveland Clinic Abu Dhabi
PO Box 112412
Abu Dhabi, United Arab Emirate

Introduction and Background

SedLine® Brain Function Monitoring provides real-time insight into a patient's depth of anesthesia with bilateral data acquisition and processing of electroencephalogram (EEG) signals. Four active EEG leads collect data from the frontal lobe with a sensor position on the patient's forehead. (1)

For frontal approach neurosurgical and neurointerventional procedures, the usual placement of the SedLine® sensor is challenging.

Numerous studies have already analyzed the accuracy of the change of position and the application of alternative positions for other devices used for depth of anesthesia monitoring (2,3,4,5). Albeit this, yet to date, there is no study that analyzed the application of alternative positions for the SedLine® sensors.

Research Questions and Hypotheses

The purpose of our study is to compare the standard Masimo SedLine EEG sensor frontal placement versus an experimental nasal placement of the SedLine® sensors for neuromonitoring. To determine whether this position generates similar data and validate this new alternate position.

We hypothesized that placing the central sensors in the montage approximately 2 cm below the standard recommended placement, across the nasal bridge and then running under the eyes to the normal temporal leads placement would put the entire montage out of the operative field and would still have corresponding values.

Study Design

Prospective cohort study.

Population

It is expected to recruit 40 patients undergoing general anesthesia. Considering a drop-out of 20%, we'll recruit 50 patients.

Duration of evaluation

Study participants will be evaluated only during surgery.

The study will be performed in an operation room during surgery, from the moment of induction to anesthesia up to a few minutes after the extubation. Setting up the sensor, time alignment in both Masimo Roots, as well as collecting and processing data from both sensors will be the standard approach for all 40 patients.

No further observation is needed.

Inclusion criteria

- Patients older than 18 years of age, both genders.
- Patients undergoing simple or complex surgery.
- American Society of Anesthesiologists Classification (ASA) score I to III.

Exclusion criteria

- American Society of Anesthesiologists Classification (ASA) score IV and V.
- Age below 18
- Previous neurological problems affecting EEG
- Dementia
- Use of sedative or drugs that can alter EEG readings
- Patients under head and neck surgery

PROCEDURES AND METHODS**Selection and recruitment of patients**

Patients are identified as potentially recruitable during the preoperative visit in the preoperative department. The anesthesiologist has to inform adequately patient. After this preliminary check for recruitment criteria, the patient will receive the informing module. The researcher confirms the recruitment criteria during the pre-surgical visit.

Data obtained during the study are confidential and during their presentation will not be discovered information that may reveal the identity of the patient.

Intervention

The authors will perform a prospective study, enrolling patients and performing neuromonitoring using both the standard (FRONTAL) and the alternative (NASAL) montage on each patient.

Evaluation

1. Primary end-point:

- We will monitor and compare processed electroencephalograph (EEG) values (PSi- Patient State Index, SEFL- Spectral Edge Frequency Left, SEFR- Spectral Edge Frequency Right, SR-Suppression Ratio, EMG-Electromyograph, ARTF-Artifact) and EEG waveforms, from nasal and frontal sensors.

2. Other data collected will include:

- Other parameters that will be measure are patient demographics (age, sex, surgery, ASA status, weight, height, BMI).

Plan of study

At least 40 patients are expected to be included after obtaining the approval of Ethical Committee. Patients will be included only if they sign informed consent for study.

The study includes a preoperative visit, perioperative observation.

STATISTICAL ANALYSIS

For each of the two modes of measurement, 1800 data points per subject (1 reading every 2 seconds for 1 hour) per hour will be collected. Assuming a maximum interclass correlation coefficient of .90, a sample size of 40 patients will be required to test the null hypotheses that the two modes of measurement share 95% of their variance via the construction of a 95% confidence interval that ranges no more than +-5%.

Analysis plan

The initial descriptive statistics will describe and summarize the patient characteristics.

Data from the 2 placements will be compared and analyzed using a Bland-Altman analysis and a matched-pair analysis.

Access to data and statistical processing of data will be available and compiled by the author of the study, Dr Boris Tufegdžić and CCAD biostatistician, Terrence Lee-St. John.

Safety

Risks and Benefits

This prospective observational cohort study does not present greater than minimal risk for patient.

There is no prospect of direct benefit but we will gain knowledge that can help us in future neuromonitoring.

Data Safeguards

We will maintain data in a secure environment; we will use only CCAD laptop computers to store the data.

There will be two levels of password protection.

Safety Cont.

Consent

Patients are identified as potentially recruitable during the preoperative visit in the preoperative department. The anesthesiologist has to inform adequately patient. After this preliminary check for recruitment criteria, the patient will receive the informing module.

The researcher confirms the recruitment criteria during the pre-surgical visit.

Data obtained during the study are confidential and during their presentation will not be discovered information that may reveal the identity of the patient.

Adverse Events and Data Monitoring Committee (DMC)

Data Monitoring Committee is not planned but we will have regular meetings between principal investigators and co-investigators. This study does not present greater than minimal risk for patient.

Sponsorship

The use of SedLine® monitoring is a standard part of everyday anesthesia practice in our institute.

Additional resources (sensors) required for this study will be provided by the sponsor, Masimo Company. Masimo is a global medical technology company that develops and manufactures innovative noninvasive patient monitoring technologies, medical devices, and a wide array of sensors.

Masimo Company will provide 50 sensors that we need as addition to ours that we use as part of standard monitoring during general anesthesia.

Masimo company will provide 50 sensors because we need to include potential drop-offs (20%). After obtaining approval from Research Ethics Committee, we will receive the Equipment Loan Agreement from Masimo Company.

Appendices

Appendix A: Medical Record Collection Form

Appendix B: Informed consent

Appendix C: Masimo - SedLine Study Approval Letter

Appendix D: Application Signature Page

References

1. <http://www.masimo.com/products/continuous/root/root-sedline/>
2. Nelson P, Nelson JA, Chen AJ, Kofke WA.: An alternative position for the BIS-Vista montage in frontal approach neurosurgical cases. *J Neurosurg Anesthesiol.* 2013 Apr; 25(2):135-42.
3. Akavipat P, Hungsawanich N, Jansin R.: Alternative placement of bispectral index electrode for monitoring depth of anesthesia during neurosurgery. *Acta Med Okayama.* 2014; 68(3):151-5.
4. Dahaba AA, Xue JX, Zhao GG, Liu QH, Xu GX, Bornemann H, Rehak PH, Metzler H.: BIS-vista occipital montage in patients undergoing neurosurgical procedures during propofol-remifentanyl anesthesia. *Anesthesiology.* 2010 Mar; 112(3):645-51.
5. Lee SY, Kim YS, Lim BG, Kim H, Kong MH, Lee IO.: Comparison of bispectral index scores from the standard frontal sensor position with those from an alternative mandibular position. *Korean J Anesthesiol.* 2014 Apr; 66(4):267-73. Epub 2014 Apr 28.

Acronyms:

1. **Suppression Ratio (SR)** - Measures how much the electrical activity of the frontal and pre-frontal cortex of the brain is suppressed as a percentage of time. This value ranges from 0 to 100%.
2. **Patient State Index (PSi)** - A processed EEG parameter related to the effect of anesthetic agents. This value ranges from 0 to 100.
3. **Spectral edge frequency (SEF)** - is the frequency below which 95 %, 90 % or 50 %, respectively, of the total EEG power is located.
4. **Artifact (ARTF)** - Measures how much physiological (not brain-related) and environmental noise the system detects. This value ranges from 0 to 100%.
5. **Electromyograph (EMG)** - Measures detected muscle activity, such as grimacing or jaw clenching. This value ranges from 0 to 100%.