VALIDITY OF BISPECTRAL INDEX MONITORING AT INFRA-ORBITAL POSITION IN REFERENCE TO THE STANDARD FRONTAL POSITION

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-Dr. Aina Ahmad Zaki-

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LIST OF SYMBOLS AND ABBREVIATIONS

ASA	American Society of Anaesthesiologist
ANOVA	Analysis of Variance
BIS	Bispectral Index Scores
BMI	Body Mass Index
CI	Confidence Interval
Cm	Centimeter
ECG	Electrocardiogram
EEG	Electroencephalography
EMG	Electromyography
ETT	Endotracheal Tube
FR	Frontal
G	Gram
GA	General anaesthesia
HUSM	Hospital Universiti Sains Malaysia
ICC	Intraclass correlation
IO	Infra-orbital
IQR	Inter-quartile range
IV	Intravenous
Kg	Kilogram
kg/m^2	Kilogram per meter squared
mcg/ml	Microgram per mililitre

mg/kg Milligram per kilogram

Ng/ml Nanogram per mililitre

NMB Neuromuscular blocker

LOC Loss of consciousness

SPSS Social Package for the Social Sciences

SD Standard Deviation

SQI Signal Quality Index

TCI Target-controlled infusion

TIVA Total Intravenous Anaesthesia

$<$ Less than

$\leq$ Equal or less than

$=$ Equal to

% Percent

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ABSTRAK

Latar belakang: Di dalam keadaan pembedahan tertentu, posisi sensor *bispectral index* (BIS) di bahagian dahi tidak selalunya dapat dilakukan kerana bacaan yang tidak tepat dapat terjadi akibat gangguan dari kawasan pembedahan atau posisi pesakit. Kajian ini adalah bertujuan untuk mengkaji pengesahsahihan bacaan BIS di bahagian bawah mata dengan kedudukan standar di dahi semasa pembiusan am secara intravena.

Kaedah: Seramai 71 pesakit yang menjalani pembedahan elektif melalui kaedah *target-controlled infusion* (TCI) menggunakan propofol dan remifentanil telah diselidiki. Setiap pesakit dilekatkan dengan dua sensor BIS di dahi dan di bawah mata. Nilai BIS diperolehi pada enam titik masa; ketika sedar, hilang kesedaran, selepas diintubasi, insisi kulit, setiap 30 minit fasa pembiusan, sewaktu mulai sedar dan ekstubasi. Data yang diperolehi di analisa dengan korelasi *Pearson* dan *intraclass*. Analisis *repeated measures* ANOVA digunakan untuk menentukan pengaruh hubungan di antara kedua posisi BIS.

Keputusan: Menerusi analisis korelasi *Pearson,* nilai BIS di kedua posisi menunjukkan korelasi positif yang signifikasi ($p<0.05$). Analisis korelasi *intraclass* mempamerkan konsistensi dalaman yang kuat pada semua titik masa dengan nilai *coefficient* 0.794. Berdasarkan *repeated measures* ANOVA, kedua posisi menunjukkan bacaan BIS yang konsisten ($p<0.001$) dan tiada perbezaan yang signifikasi pada purata bacaan BIS di kedua posisi ($p=0.809$). Bacaan BIS pada setiap titik masa tidak dipengaruhi oleh posisi sensor ($p=0.173$).

Kesimpulan: Bacaan BIS di bahagian bawah mata adalah konsisten dengan di dahi dan ia dapat dijadikan alternatif untuk memeriksa tahap kesedaran semasa pembiusan am secara intravena apabila posisi di dahi tidak memungkinkan.

Kata kunci: alternatif, bispectral index, frontal, infra-orbital, pembiusan am intravena

ABSTRACT

*Background***:** In certain surgery, the placement of frontal BIS is not always possible as it may give inaccurate readings due to the interference from operation site or patient's position. This study aimed to validate the BIS values obtained from the alternative infra-orbital sensor position in relation to standard frontal area during total intravenous anaesthesia (TIVA).

*Methods***:** A total of 71 patients who underwent elective surgery under target-controlled infusion (TCI) propofol and remifentanil were recruited. Each patient had two BIS sensors placed at their forehead and infra-orbital. BIS values were obtained at six timepoints; during awake, loss of consciousness, post intubation, skin incision, every 30 minutes during maintenance of anaesthesia, emergence and extubation. Data from both BIS sensors were compared using Pearson's correlation and intraclass correlation (ICC). Repeated measures analysis of variance (ANOVA) was used to determine the relationship between the two positions.

Results: Pearson's correlation analysis showed positive correlation ($p<0.05$) for both positions. Analysis of ICC revealed strong internal consistency across all timepoints with coefficient value of 0.794. According to repeated measures ANOVA, both positions showed consistent trend in BIS values ($p <0.001$) with no significant difference in the mean readings ($p=0.809$). The BIS readings at different timepoints were not affected by the position of the probe ($p=0.173$).

Conclusion: The infra-orbital BIS is consistent with frontal BIS monitoring and it can be an alternative to monitor depth of anaesthesia during TIVA whenever the standard frontal position is impossible.

Keywords: alternative, bispectral index, frontal, infra-orbital, total intravenous anaesthesia

CHAPTER 1

INTRODUCTION

Background

Bispectral index (BIS) is a complex electroencephalography (EEG) parameter that converts raw EEG data from the frontal cortex into a single dimensionless number ranging from 0 to 100(1). They are the result of two innovations: bispectral analysis and BIS algorithm derived from the analysis of large number of EEGs of volunteers and patients (more than 5,000 adult subjects) under sedation and general anaesthesia with different anaesthetics (2). In non-anaesthetized patients the BIS varies from 90 to 100. On the other hand, total suppression of cortical electrical activity results in a BIS of zero (isoelectric EEG) (2). A BIS between 40 and 60 is an acceptable depth of hypnosis and associated with a low probability of intraoperative awakening and awareness during general anaesthesia (2,8,11).

The BIS device consists of a transducer that's connected to a monitor on one end and the patient's forehead via an adhesive electrode sensor strip on the other (3). The two to four sensors on the strip each have numbers that indicate where on the forehead they should be placed for optimal EEG signal analysis (3). The EEG signal is subsequently digitised, amplified and filtered to isolate EEG from other biological potentials such as ECG waveforms, ocular activity and mains power interference (3). The monitor calculates the data received by the sensors and displays this information as a numeric value from 0 to 100 with a 10- to 30-second time delay (4). Most BIS systems also displayed a graphical trend which represent the ongoing

calculations of the BIS index during the case (3).

BIS measures only the hypnotic component of anaesthesia, representing the degree of alertness and it does not measure the concentration of a particular drug (5). Anaesthetic techniques consisting of a low or moderate dose of an opioid and a hypnotic drug are the most accurately represented with BIS monitoring (3). BIS monitoring has been shown to be less reliable in anaesthetics involving higher-dose opioids and is insensitive to several commonly used anaesthetic agents such as ketamine and nitrous oxide(6,11).. Electromyography (EMG) activity contributes to ~20% of the BIS values in the higher ranges (4,15). Elevated EMG activity increases BIS, while the subsequent administration of neuromuscular blockers (NMBs) reduces it (2,15,17).

Monitoring of the BIS allows the reduction of anaesthetics, maintenance of adequate levels of hypnosis, and prevents both extremely deep anaesthesia levels and awakening and formation of implicit and explicit memory during general (3,15,19). It also allows faster awakening and reduces the length of stay in the post-anaesthetic recovery room, which reduces costs (2.19).

The standard frontal BIS placement for certain surgical procedures may not be possible as it can interferes with the operative field. For example, in neurosurgical procedures that would require a frontal approach might be an impediment for a successful frontal BIS sensor placement (4,18,20). Apart from that, patient's position such as prone or lateral may lead to problem in monitoring BIS (7,16).

Study conducted by Nelson P. *et al* in 2013 compared the BIS values at frontal and nasal dorsum sensors position in neurosurgical patients under TIVA. The Bland-Altman analysis revealed a difference in score of -2.0 (95% confidence interval, -

14.1, 10.1), with 108/2567 (4.2%) of the values lying outside of the limit of agreement (8). The scatter plot analysis overall produced a trend line with the equation y=0.94x+0.82, with an R coefficient of 0.82. As a conclusion, they found that the nasal montage produces values that have slightly more variability compared with that ideally desired, but the variability is not clinically significant (8).

One study conducted in Korea, by Shin YL et al published in 2014 compared the BIS scores between frontal and submandibular sensors position during general anaesthesia (GA) using inhalational agents. 58 patients scheduled for various surgical procedures not involving the head or neck were enrolled in this study (1). Scatter plot analysis revealed a significant correlation between BIS values of frontal and mandibular positions (R = 0.869, P = 0.000), except during emergence (R = 0.253, P = 0.077)(1). From this study, they found that overall, BIS values do not agree between the standard frontal position and an alternative mandibular position except during the anaesthesia maintenance period (1).

Another study published in 2014 by Phuping A. *et al* compared BIS readings placed at both frontal and post- auricular areas in 34 patients scheduled for neurosurgery under GA using TIVA (7). The BIS values and impedance were recorded; Pearson’s correlation and Bland-Altman plots were analysed. The bias ± 2SD for the electrode placement before, during, and post-anaesthesia were 0±23.32, 1.5±10.69, and 2.1±13.52, while the limits of agreement were −23.3 to 23.3, −12.2 to 9.2, and −17.7 to 13.5, respectively (7). The correlation coefficient between frontal and post-auricular area electrodes was 0.74 with a p-value ＜0.001

(7). The conclusion showed post-auricular placement of a BIS electrode is a practical alternative to frontal lobe placement (7)

Study by Brown B. *et al* in 2014 assessed the acceptability of auricular versus frontal BIS. The result demonstrated that the limits of agreement are too wide for auricular approach to be used in substitution of the frontotemporal approach (13).

Hajiveya K. *et al* in 2017 found that nasal dorsum sensor can be a good and safe alternative to standard frontal measurements in neurosurgery patient under TIVA (6). Another case report showed good depth of anaesthesia monitoring resulting from spectral entropy during a craniotomy with aneurysm clipping when the sensors were placed at the occipital area (18)

On the other hand, one study by Dahaba *et al.*in 2010 demonstrated significant differences between BIS values from the frontal and occipital placement of BIS-Vista sensors before induction and at maintenance of anaesthesia (11).

In 2018, Puente B. *et al* compared the concordance between BIS values depending on the frontal or infra-orbital placement of the sensor in 48 adult patients undergoing laparascopic abdominal surgery under GA inhalation. The results showed the variability between BIS recordings obtained from the 2 sensors was acceptable for clinical use (9). The infra-orbital BIS sensor setup could be an adequate alternative for cases in which the frontal setup is not possible (9).

Rationale of the Study

Although several alternative sensor positions have been examined in the past, there remains significant disagreement over their reliability. Besides that, previous studies were done with different anaesthetics techniques that used either inhalational

agents or TIVA. Therefore, this study aims to validate the BIS values obtained from the alternative infra-orbital sensor position in reference to the standard frontal position to monitor depth of anaesthesia during TIVA, which has never been reported yet.

Study Objectives

General Objective

To determine the correlation of BIS values obtained from the standard frontal sensor position and the alternative infra-orbital sensor position during TIVA.

Specific Objectives

1. To determine the correlation of BIS values obtained from frontal sensor versus infra-orbital position during TIVA at different time points, which are at awake, loss of consciousness, post intubation, skin incision, every 30 minutes during maintenance period of anaesthesia, emergence at which propofol plasma concentration 1.5mcg/ml and at extubation.
2. To determine the relationship of BIS values obtained from frontal sensor versus infra-orbital position during TIVA at different time points, which are at awake, loss of consciousness, post intubation, skin incision, every 30 minutes during maintenance period of anaesthesia, emergence at which propofol plasma concentration 1.5mcg/ml and at extubation.

Null Hypotheses

1. There is no correlation between BIS values obtained from infra-orbital sensor and frontal sensor position.

2. There is no relationship between BIS values obtained from infra-orbital sensor and frontal sensor position.

Alternative Hypotheses

1. There is a correlation between BIS values obtained from infra-orbital sensor and frontal sensor position.
2. There is a relationship between BIS values obtained from infra-orbital sensor and frontal sensor position.

CHAPTER 2

METHODOLOGY

Study Design

Prospective, cross-sectional study.

Setting

Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan.

Study Period

1-year period.

Study Population

Patients undergoing all types of elective surgery under TIVA in Hospital Universiti Sains Malaysia (HUSM), Kubang Kerian, Kelantan, Malaysia.

Inclusion Criteria

- Age between 18 years old to 60 years old.
- ASA physical status I or II.
- BMI > 18 and <30 kg/m^2.

Exclusion Criteria

- Neurosurgery, maxillofacial or facial surgical procedures.
- Patients with a history of disabling central nervous or cerebrovascular disease.
- Patients on central nervous system active drugs or psychiatric medication.
- Patients who had neurosurgical procedure.

- Pregnant.
- Allergy to the study drugs.
- Patients who are unable to give consent for themselves.

Withdrawal criteria

- Subjects may be withdrawn if investigator deems that is detrimental or risky for subjects to continue the study. For example, if the subject has massive bleeding or hemodynamically unstable or require intensive care and ventilatory support post operation.

Sampling Method

The estimated frequency for procedure done under TIVA is 10 cases per month. Within 1-year duration of the study, there will be about 120 cases. Therefore, no sampling method is applied. All types of elective surgery under TIVA that fit all the criteria will be included in this study.

Sample Size Estimation

To estimate the sample size required for our study, we utilized the PS Power and Sample Size Calculations and G*Power software.

- In order to determine the correlation between BIS values obtained from frontal versus the infra-orbital sensor position, using Pearson's correlation, the sample size will be determined with parameter of effect 0.3, an alpha of 0.05 and a power of 80%. The sample size required is 64 patients (Figure 2). For intraclass correlation (ICC), the sample size required is 27 patients (Figure 3).

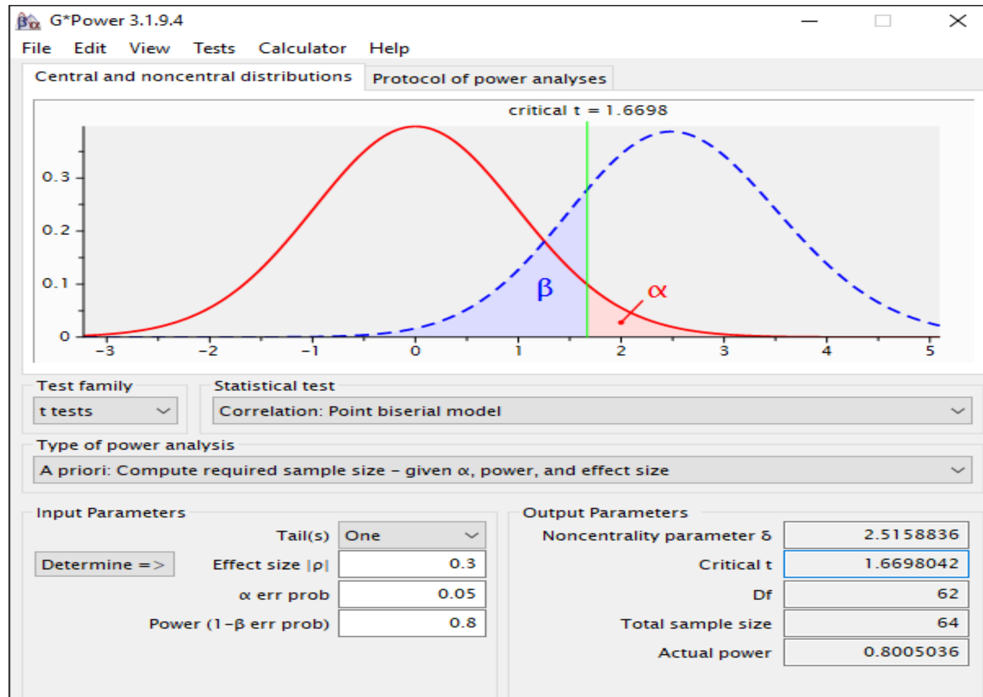

Figure 1: Sample size calculation for Pearson's correlation.

D1	Intraclass Correlation		
	Observation/Subject (n)	6	Number of repeated observations by different judges per subject, replicates
	Significance level (α)	0.050	Two-tailed
	Power (1-β)	0.800	
	Minimum acceptable reliability (ρ_0)	0.60	The lowest limit of reliability you would accept
	Expected reliability (ρ_1)	0.80	The level of reliability you can expect from the study
	Drop-out	10%	
	Sample size	24	
	Sample size (with drop-out)	27	
Reference:	Walter, S.D., Eliasziw, M., Donner, A. (1998). Sample size and optimal designs for reliability studies. Statistics in medicine, 17, 101-110.	D1	

Figure 2: Sample size calculation for intraclass correlation.

- In order to determine the relationship between BIS values obtained from frontal versus the infra-orbital sensor position, using repeated measures

ANOVA, the sample size will be determined with parameter of effect size 0.17, an alpha of 0.05 and a power of 80%. The sample size required is 36 patients (Figure 3).

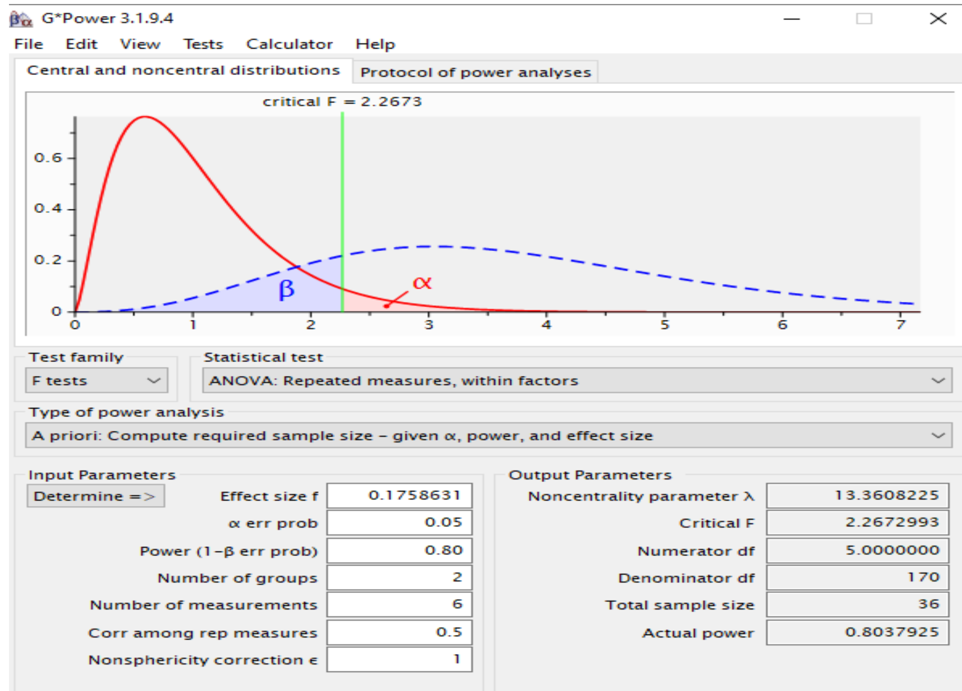

Figure 3: Sample size calculation for repeated measures ANOVA.

Based on all the required statistical analysis, the final sample size is 71 patients which included the estimation of 10% drop-out rate.

Research Tools

- Search databases: "Research Gate", "Pubmed", "Google Scholar".
- Designed data form to assist data collection process.

Operational Definitions

- Dependent variables: BIS values taken at 6 timepoints; at awake, loss of consciousness, after intubation, after the start of surgical incision, every 30 minutes during the intraoperative period (maintenance), after cessation of TCI at which the plasma concentration of propofol is 1.5mcg/ml (emergence) and at extubation. BIS values for maintenance of anaesthesia will be taken as mean.
- Loss of consciousness is defined as loss of eyelash reflex.
- Extubation is defined as the removal of endotracheal tube from patient's mouth.
- A single BIS value will be collected at each timepoints
- Clinically acceptable level "limit of agreement" is 10 BIS units according to the previous study [1].
- Independent variables: BIS sensor locations which are at frontal and infraorbital region.
- Standardized BIS™ Quatro sensors and BIS Vista™ monitors will be used for this study.

Data collection method

- Coding-decoding system will be used.
- No premedication is prescribed prior to surgery.
- In the operation theatre, before induction of anaesthesia, standard monitoring such as non-invasive blood pressure, ECG, pulse oximeter will be applied.
- 2 BIS™ Quatro sensors will be applied to each patient, 1 across the forehead while the other at the infra-orbital position and will be connected to each BIS Vista™ monitors.

- Frontal sensors will be applied with circle 1 at the centre of forehead, circle 2 2.8cm lateral to circle 1, circle 3 on the corner of the eye and circle 4 between circle 2 and 3.
- Infra-orbital sensors will be applied with circle 1 across the nose bridge, circle 2 adjacent to circle 1, circle 3 medial from the frontally placed third electrode and circle 4 between circle 2 and 3.
- Both BIS™ Quatro sensors placement should be checked as not to interfere with the operative field.
- During surgery all of them will be induced by standard protocol.
- Induction:
    - ✓ Patients will be pre-oxygenated for 3-5 minutes or until end-tidal oxygen fraction of 85 is achieved.
    - ✓ Induction with TCI remifentanil initial target concentration at 2ng/ml up to 4ng/ml, TCI propofol at initial target concentration at 4mcg/ml and titrate upwards to loss of consciousness and IV rocuronium 0.6 – 1.2mg/kg for endotracheal tube (ETT) placement.
- Maintenance:
    - ✓ Patient will be ventilated with mixture of oxygen and air. Maintenance of anaesthesia with total intravenous anaesthesia (TIVA); infusion of propofol at target plasma concentration 3-6mcg/ml and remifentanil 1-8ng/ml.
    - ✓ Intra-operative analgesia; IV paracetamol 1g, IV parecoxib 40mg and IV morphine 0.05-0.1mg/kg.

- Reversal:
    - ✓ IV neostigmine 0.05 mg/kg and atropine 0.02mg/kg
- TIVA will be guided by frontal BIS for monitoring depth of anaesthesia.
- The stages of hypnosis; deep (BIS < 45), moderate (BIS 45 to 60) and mild (BIS >60) will be established.
- BIS values from each BIS Vista™ monitor will be collected into the designed form at awake, at loss of consciousness, after intubation, after the start of surgical incision, every 30 minutes during the intraoperative period (maintenance), after cessation of TCI at which the plasma concentration of propofol is 1.5mcg/ml (emergence) and at extubation.
- Data collection form will be compiled into a file and labelled properly.

Proposed Data Analysis

Data will be analysed using SPSS version 26. Descriptive statistics will be used to summarize the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normal distribution. Categorical data will be presented as number of percentages.

Statistical analysis to evaluate the concerned specific objectives for this study would be using Pearson's correlation, intraclass correlation and repeated measures ANOVA analysis.

Expected Results.

Table 1. Patient's demographic (n= 71).

Category	Number (%)	Mean ± SD
Age (years)		
Gender		
ASA I/II		
BMI (kg/m^2)		
Types of surgery		
Duration of surgery (minutes)		

Table 2. Pearson's correlation of BIS values obtained from frontal versus infra-orbital (n= 71).

BIS Readings	r (95% CI)	P value
Awake		
LOC		
Post-intubation		
Skin Incision		
Maintenance of anaesthesia		
Emergence		
Extubation		

Table 3. Intraclass correlation (ICC) of BIS values obtained from frontal vs. infra-orbital (n= 71).

BIS Readings	r (95% CI)	P value
Awake		
LOC		
Post-intubation		
Skin Incision		
Maintenance of anaesthesia		
Emergence		
Extubation		

Table 4: Repeated ANOVA analysis of BIS values at different timepoints within and between study groups.

Variables	DF	F	P value
BIS Value Within Subject Effect			
Time			
Time*Group			
Between Subject Effect			
Group			

Gantt Chart

The Gantt Chart of this study is presented in Figure 4 below.

YEAR	2020												2021												2022				
MONTH	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M
Proposal Planning																													
Proposal Defense																													
Ethics Submission																													
Data Collection																													
Data Analysis																													
Thesis Write-up																													
Supervisor Review																													
Thesis Submission																													

Figure 4: The Gantt chart.

Flow Chart of the Study

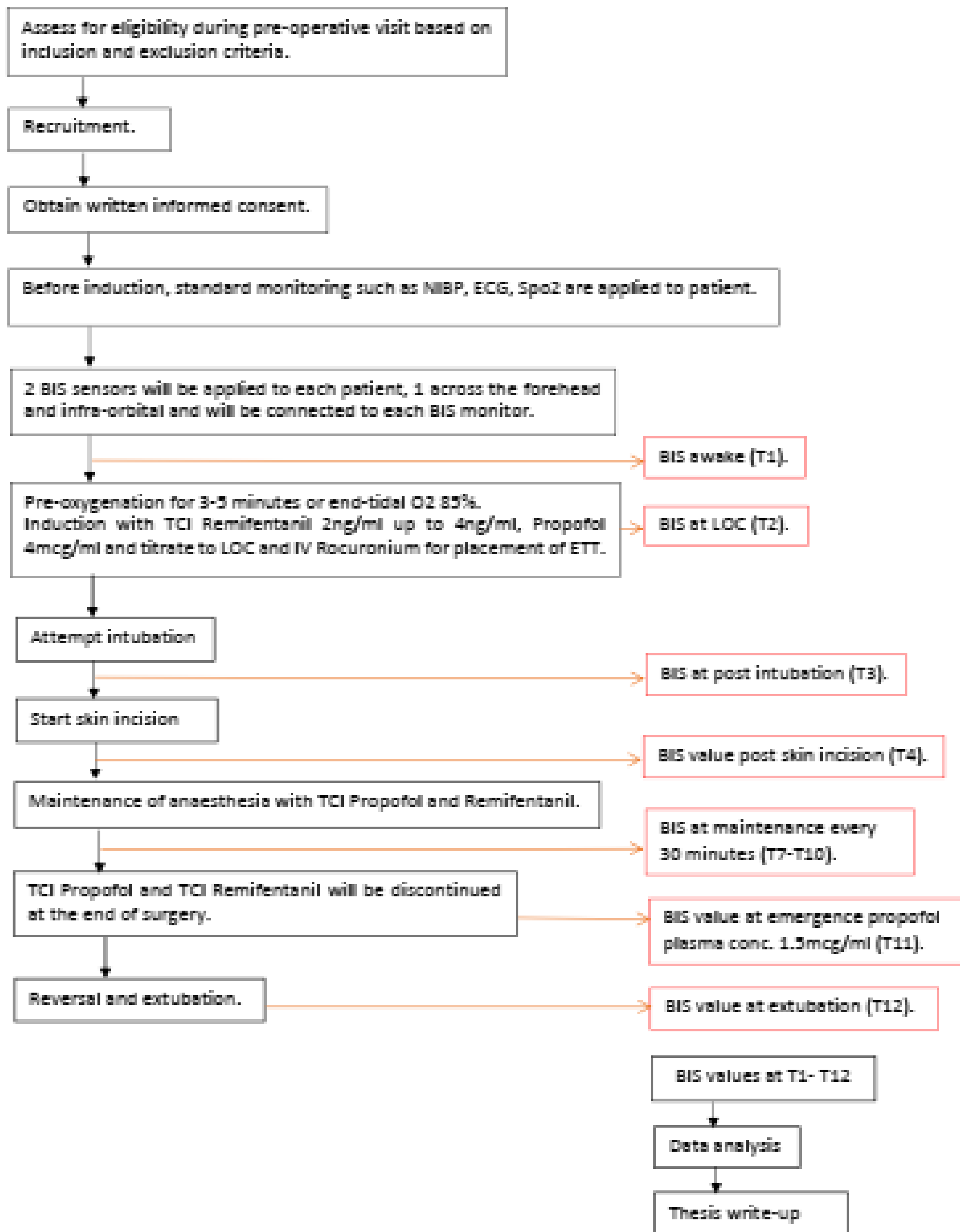

Figure 5: Study flow chart

Ethical Consideration

Subject Vulnerability

- Patients who are unable to give consent for themselves will be excluded, such as with learning disabilities, cognitive dysfunction and there is susceptibility to coercion.
- Other patients will full capacity to give consent will be given full freedom to participate or refuse with assurance that his/her medical treatment will not differ otherwise.
- There are no serious side effects known to be caused by the investigational product.

Declaration of Absence of Conflict of Interest

- There are no serious side effects known to be caused by the investigation.
- This study is not sponsored or influenced by any medical or drug representative.
- Investigator will not be receiving any incentive from BIS associated company.

Privacy and Confidentiality

- All forms are anonymous and will be entered into SPSS software.
- Data will be represented as grouped data and will not identify the responder individually.

Community sensitivities and benefits

- Study findings shall improve means of monitoring depth of anaesthesia during situation in which standard BIS sensor position is not possible.

- The expected benefit outweighs the minimal risk to subjects and thus this study should be supported.

Honorarium and incentives

- No honorarium or incentive will be given to the patients.

Ethical Approval Letter

Jawatankuasa Etika
Penyelidikan Manusia USM (JEPeM)

Human Research Ethics Committee USM (HREC)

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1st November 2020

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JEPeM Code : USM/JEPeM/20060307
Protocol Title : Comparative Study of Bispectral Index (BIS) Values Obtained from Standard Frontal Position and Alternative Infra-Orbital Position during Total Intravenous Anaesthesia (TIVA).

Dear Dr.,

We wish to inform you that your study protocol has been reviewed and is hereby granted approval for implementation by the Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM). Your study has been assigned study protocol code **USM/JEPeM/20060307**, which should be used for all communications to JEPeM-USM in relation to this study. This ethical approval is valid from **1st November 2020** until **31st October 2021.**

Study Site: Hospital Universiti Sains Malaysia.

The following researchers are also involved in this study:
1. Dr. Mohamad Hasyizan Hassan
2. Dr. S. Praveena a/p Seevaunnamtum

The following documents have been approved for use in the study.
1. Research Proposal

In addition to the abovementioned documents, the following technical documents were included in the review on which this approval was based:
1. Patient Information Sheet and Consent Form (English version)
2. Patient Information Sheet and Consent Form (Malay version)
3. Data Collection Form

The list of JEPeM-USM members present during the full board meeting reviewing your protocol is attached.

While the study is in progress, we request you to submit to us the following documents:
1. Application for renewal of ethical approval 60 days before the expiration date of this approval through submission of **JEPeM-USM FORM 3(B) 2019: Continuing Review Application Form.**
2. Any changes in the protocol, especially those that may adversely affect the safety of the participants during the conduct of the trial including changes in personnel, must be submitted or reported using **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**
3. Revisions in the informed consent form using the **JEPeM-USM FORM 3(A) 2019: Study Protocol Amendment Submission Form.**

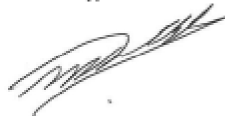
4. Reports of adverse events including from other study sites (national, international) using the **JEPeM-USM FORM 3(G) 2019: Adverse Events Report.**
5. Notice of early termination of the study and reasons for such using **JEPeM-USM FORM 3(E) 2019.**
6. Any event which may have ethical significance.
7. Any information which is needed by the JEPeM-USM to do ongoing review.
8. Notice of time of completion of the study using **JEPeM-USM FORM 3(C) 2019: Final Report Form.**

Please note that forms may be downloaded from the JEPeM-USM website: **www.jepem.kk.usm.my**

JEPeM-USM is in compliance with the Declaration of Helsinki, International Conference on Harmonization (ICH) Guidelines, Good Clinical Practice (GCP) Standards, Council for International Organizations of Medical Sciences (CIOMS) Guidelines, World Health Organization (WHO) Standards and Operational Guidance for Ethics Review of Health-Related Research and Surveying and Evaluating Ethical Review Practices, EC/IRB Standard Operating Procedures (SOPs), and Local Regulations and Standards in Ethical Review.

Thank you.

Sincerely,



PROF. DR. HANS AMIN VAN ROSTENBERGHE
Chairperson
Jawatankuasa Etika Penyelidikan (Manusia) JEPeM
Universiti Sains Malaysia

CHAPTER 3

MANUSCRIPT

Title

Validity of Bispectral Index Monitoring at Infra-orbital Position In Reference To The Standard Frontal Position

Running head

Infra-orbital versus frontal bispectral index scores (BIS)

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Abstract

Background: In certain surgery, the placement of frontal BIS is not always possible as it may give inaccurate readings due to the interference from operation site or patient's position. This study aimed to validate the BIS values obtained from the alternative infra-orbital sensor position in relation to standard frontal area during total intravenous anaesthesia (TIVA).

Methods: A total of 71 patients who underwent elective surgery under target-controlled infusion (TCI) propofol and remifentanil were recruited. Each patient had two BIS sensors placed at their forehead and infra-orbital. BIS values were obtained at six timepoints; during awake, loss of consciousness, post intubation, skin incision, every 30 minutes during maintenance of anaesthesia, emergence and extubation. Data from both BIS sensors were compared using Pearson's correlation and intraclass correlation (ICC). Repeated measures analysis of variance (ANOVA) was used to determine the relationship between the two positions.

Results: Pearson's correlation analysis showed positive correlation ($p<0.05$) for both positions. Analysis of ICC revealed strong internal consistency across all timepoints with coefficient value of 0.794. According to repeated measures ANOVA, both positions showed consistent trend in BIS values ($p <0.001$) with no significant difference in the mean readings ($p=0.809$). The BIS readings at different timepoints were not affected by the position of the probe ($p=0.173$).

Conclusion: The infra-orbital BIS is consistent with frontal BIS monitoring and it can be an alternative to monitor depth of anaesthesia during TIVA whenever the standard frontal position is impossible.

Keywords: alternative, bispectral index, frontal, infra-orbital, total intravenous anaesthesia