

AUTOMATED PUPILLOMETRY FOR ASSESSING EMERGENCE FROM ANAESTHESIA IN SUPRATENTORIAL CRANIOTOMY PATIENTS: A PROSPECTIVE OBSERVATIONAL STUDY

Dr Revikrishnan S

PDF THESIS

DECEMBER 2024



**SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM**

An Institution of National Importance established by an Act of the Indian Parliament (Act No.52 of 1980)

Dept. of Science and Technology, Govt. of India
www.sctimst.ac.in

**Automated Pupillometry for Assessing Emergence
from Anaesthesia in Supratentorial Craniotomy Patients: A
Prospective Observational Study**

A THESIS SUBMITTED BY

Dr Revikrishnan S

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

**POST DOCTORAL FELLOWSHIP IN PERIOPERATIVE
NEUROMONITORING AND NEUROSURGICAL INTENSIVE CARE**

2024

DECLARATION BY THE STUDENT

CERTIFICATE

I, Revikrishnan S hereby certify that I had personally carried out the work depicted in the thesis titled, “**Automated Pupillometry for Assessing Emergence from Anaesthesia in Supratentorial Craniotomy Patients: A Prospective Observational Study**”

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.

Signature

Date.

Name of the Candidate

CERTIFICATE BY THE RESEARCH GUIDE

Name of the Guide: Dr Manikandan S

Division : Neuroanesthesia and Critical care

This is to certify that Revikrishnan S, Division of Neuroanesthesia and critical care of this institute has fulfilled the requirements prescribed for the Post Doctoral Fellowship in Perioperative Neuromonitoring and Neurosurgical Intensive Care, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.

The thesis entitled, “Automated Pupillometry for Assessing Emergence from Anaesthesia in Supratentorial Craniotomy Patients: A Prospective Observational Study” was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

Clearance was obtained from the Institutional Ethics Committee for carrying out the study.

Signature

Date.

Name of the Guide

APPROVAL OF THE THESIS

The thesis entitled

**Automated Pupillometry for Assessing Emergence from Anaesthesia in
Supratentorial Craniotomy Patients: A Prospective Observational Study**

Submitted by

Dr Revikrishnan S

for the degree of

**POST DOCTORAL FELLOWSHIP IN PERIOPERATIVE
NEUROMONITORING AND NEUROSURGICAL INTENSIVE CARE**

**SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM**

is evaluated and approved by

.....

(Name & Signature of the Guide)

ACKNOWLEDGEMENTS

Working on this thesis has been a great learning experience for me. I would like to thank a number of people who have contributed to the final result in many different ways.

I express my sincere gratitude to my guide, Prof (Dr.) Dr. Manikandan S, Professor and Head of the Division of Neuroanesthesia and Neurocritical Care, Department of Anesthesiology, SCTIMST who ploughed through several preliminary versions of my text, making critical suggestions and posing challenging questions. His expertise, invaluable guidance, constant encouragement, affectionate attitude, and healthy criticism added considerably to my experience. Without her continual inspiration, it would not have been possible to complete my study.

I am extremely grateful to Dr Ranganatha Praveen C S , Associate Professor, Neuroanesthesia division, Department of Anesthesiology, SCTIMST who was always there to improve upon my ideas and help me frame the writing work right from submitting the study protocol in the beginning to the thesis project till the end.

I'd like to express my gratitude to Dr. Smita V, Professor, Division of Neuroanesthesia and Neurocritical Care, Department of Anaesthesiology, SCTIMST, for her unwavering support and encouragement during my research.

A special word of gratitude is due to Dr. Unnikrishnan P. for their valuable advice, constructive criticism and generous help.

I am grateful and express my sincere thanks to the honourable members of the Institute Ethics Committee for approving my research protocol.

I deeply appreciate the contributions of my residents, especially Dr. Anjane Sree and the junior members, for their unwavering support, timely motivation, compassionate attitude, and consistent assistance throughout my studies.

I shall fail in my duties if I do not acknowledge my deep gratitude to all those patients who volunteered themselves as subjects for this study.

The Neurosurgery Operation Theatre and Neuro-Surgical Intensive Care Unit (NSICU) teams were always helpful despite the busy routine. The nurses and doctors went out of their way to make sure that the information required for the study was collected without a hitch.

I owe my deepest gratitude to my wife, Dr. Anjali M Panicker for her patience and unconditional support for my academic endeavours over the past several years.

TABLE OF CONTENTS

Sl.No	Title	Page No.
1.	Introduction	1 - 3
2.	Literature Review	4 - 32
3.	Material and Methods (Including Statistical analysis)	33 – 40
4.	Results	41 - 69
5	Discussion	70 - 82
6.	Summary and Conclusion	83 - 84
7.	Bibliography	84 - 90
8.	Annexures Proforma Consent English Consent Malayalam Patient Information sheet(English) Patient Information sheet(Malayalam) IEC Clearance letter Plagiarism Check Master Chart	91

LIST OF FIGURES

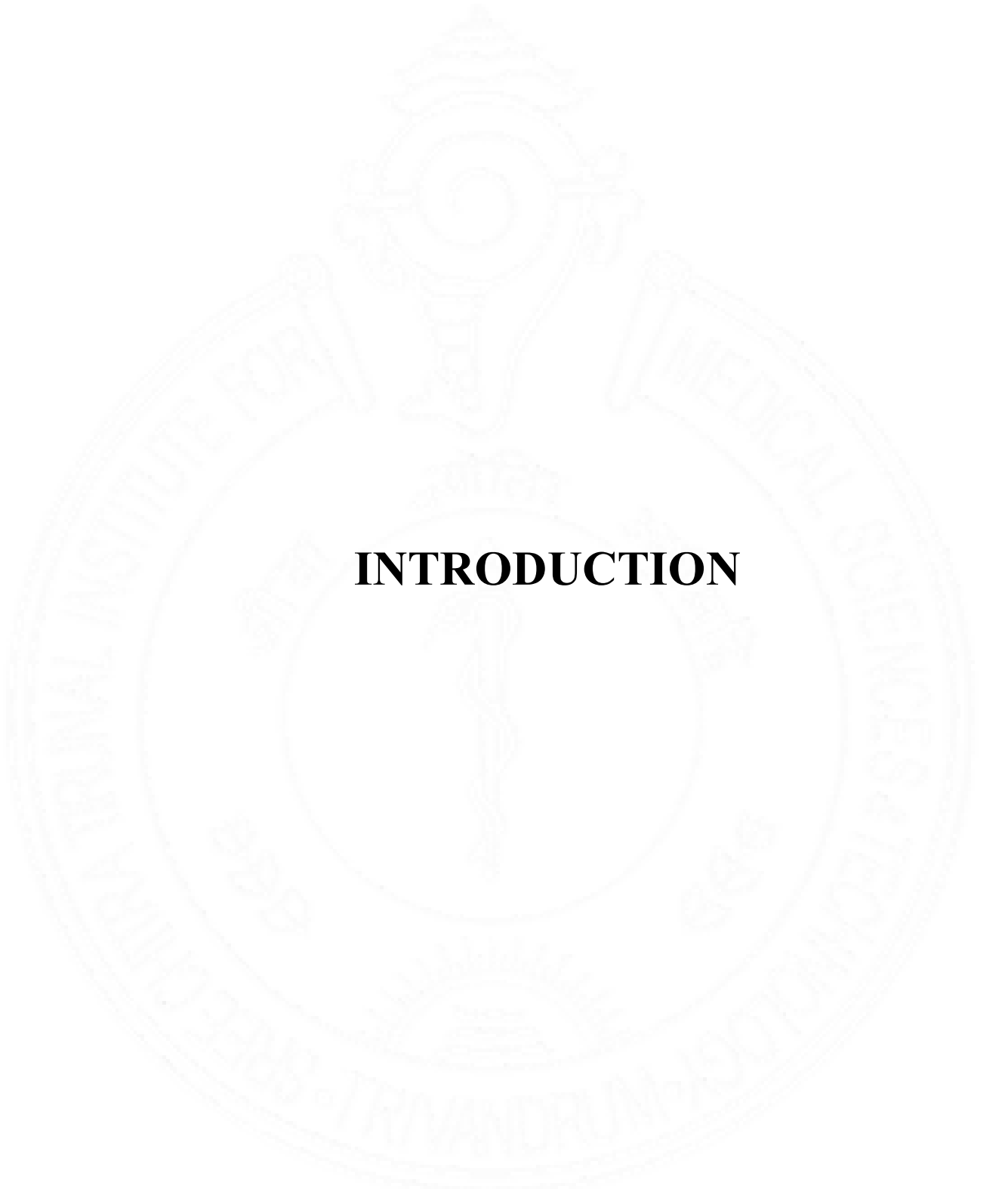
Fig. No.	Figure Captions	Page No.
Fig 1	Flow chart presenting the enrolment, study inclusion, and data analysis	41
Fig 2	Gender distribution of the subjects	42
Fig 3	ASA grading distribution of subjects)	43
Fig 4	Age distribution of subjects	43
Fig 5	Comparison of HR and MAP velocities at different time points	46
Fig 6	Comparison of TCD velocities at different time points	53
Fig 7	Comparison of CVRi, THRR and ONSD at different time pointts	62

LIST OF TABLES

Table No.	Table Captions	Page No.
1	Effects of different antihypertensives on cerebral hemodynamics.	8
2.	Demographic details of subjects	42

LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1	ANOVA	Analysis of variance
2	ASA	American Society of Anesthesiology
5	CBV	Cerebral Blood Volume
7	CPP	Cerebral perfusion pressure
8	CO ₂	Carbon dioxide
9	CT	Computed Tomography
10	CV	Cerebro-vascular resistance
11	DBP	Diastolic Blood Pressure
12	ETCO ₂	End-tidal carbon dioxide
13	HR	Heart rate
14	ICP	Intracranial pressure
15	MAP	Mean arterial pressure
16	PaCO ₂	Partial pressure of carbon dioxide
17	PaO ₂	Partial pressure of oxygen
18	SaO ₂	Saturation of arterial oxygen
19	SD	Standard deviation
20	SpO ₂	Saturation of peripheral oxygen
21	SPSS	Statistical package for social sciences



INTRODUCTION

1. Introduction

Emergence from anaesthesia is the process of regaining consciousness and normal functions after general anaesthesia.(1) The signs of emergence from anaesthesia may vary depending on the type and dose of anaesthetic agents, the patient's condition, and the method of monitoring (1). Emergence from anaesthesia should be monitored carefully and managed appropriately to ensure patient safety, especially in neurosurgical patients (1). Identifying emergence in neurosurgical patients is important for several reasons:

- Emergence can indicate the recovery of brain function and the absence of neurological complications after neurosurgery.(2)
- Emergence can enable early extubation of the patient and the transfer to the post-anaesthesia care unit (PACU) or the intensive care unit (ICU), where further monitoring and treatment can be provided. (3)

Increase in the bispectral index (BIS), which is a derived EEG parameter that measures the level of hypnosis.(4) A BIS value above 80 indicates emergence from anaesthesia, while a value between 40 and 60 usually implies adequate hypnosis without possible recall.(5) It should be emphasized that these alterations in the brain's intrinsic activity may not transpire in a synchronized or straightforward manner and can be impacted by a multitude of factors, such as the rate at which they

manifest, the existence of discomfort or stimuli, and the electromyographic (EMG) activity.(6)F

Spectral edge frequency (SEF) measures the frequency below which a certain percentage of the power spectrum of an EEG signal is concentrated and has been shown to be associated with the emergence from anaesthesia.(7) However, the identification and interpretation of EEG signatures necessitate a considerable amount of clinical expertise, which entails a deep understanding and knowledge of the intricacies involved in this complex field. Moreover, it is important to note that the application of frontal EEG and BIS in specific clinical contexts, such as neurosurgical cases that involve frontal craniotomy, can be challenging. Automated pupillometry, due to its user-friendly nature and capacity to yield objective metrics, can prove to be advantageous in circumstances of this nature.(8) Jeung Eun Kum et al investigated the pupillary changes under isoflurane anaesthesia simultaneously with the electroencephalogram (EEG) and electromyogram (EMG).(9) The authors concluded that pupil diameter precedes electrophysiological change of the brain during a transitional state of anaesthesia, and pupillometry may offer a noncontact monitoring tool for indexing the transitional state of the brain. (9) There is a paucity of literature on the utilization of pupillometry in assessing the emergence of neurosurgical procedures. Consequently, we have made the decision to strategize and execute a study to address this gap. The primary objective was to assess the correlation between changes in pupillometric indices (pupillary size, constriction velocity, and latency time) and changes in BIS during the emergence of general anaesthesia. As a secondary objective, the study assessed the correlation of change in pupillometric indices to changes to spectral edge frequency obtained from frontal

EEG during emergence from general anaesthesia. We hypothesized that the changes in pupillary reflexes measured using automated pupillometry seen during the emergence of patients from general anaesthesia who undergo supratentorial craniotomies correlate with frontal EEG changes and Bispectral index values.



LITERATURE REVIEW

2. Literature Review

Emergence from anesthesia (AE) is the ending stage of anesthesia featuring the transition from unconsciousness to complete wakefulness and recovery of consciousness (RoC)[1]. Although smooth and safe emergence is a primary target of anesthesia, during this critical phase a wide range of undesirable complications may occur. These AE complications include coughing, which may induce an increase in intracranial and intraocular pressures, respiratory events (e.g., laryngospasm) resulting in oxygenation problems, hypertension, and tachycardia as well as mental status changes such as emergence delirium (ED)[2], and delayed RoC (i.e., hypoactive emergence)[3].

From a neurobiological perspective, AE and RoC processes should not be simply considered as reverse events occurring in the induction of anesthesia. In mathematical terms, this non-linear system between induction and AE mechanisms represents a fascinating neurobiological example of “hysteresis”; thus, anesthesia can be ideally compared as a travel with a forward way (induction) which differs from that of the return (emergence). Recently, several research groups have demonstrated that the anesthetics-induced transition from wakeful state to loss of consciousness

(LoC), and vice versa the RoC phase are subjected to the control of distinct neural circuits[4,5].

2.1 NEUROBIOLOGY OF EMERGENCE

1 Mechanisms of emergence

Explanation of these mechanisms presupposes the knowledge of the action mechanisms of anesthetics, namely the neural correlates of anesthetics-induced unconsciousness. Although it does not represent the primary goal of this work, here we will try to underline the most recent pieces of evidence on the topic[6-9]. This extremely complex matter can be simplified by assuming that anesthetics interfere with cortical and subcortical signals, inducing, in turn, changes in the functional/effective connectivity across brain regions. During general anesthesia, alterations in functional and effective connectivity from different brain regions (e.g., from frontal to parietal regions) have been widely demonstrated[9]. For instance, inhalation anesthetic agents impair frontal-posterior interactions by interfering with the gamma (20-60 Hz) oscillations which have a key role in arousal and maintenance of consciousness[10]. High-density electroencephalography (hd-EEG) demonstrated that propofol-induced LoC is characterized by an increase in frontal delta power as the result of cortical propagation of processes starting from subcortical regions (e.g., lateral sulci and cingulate gyrus)[11]. In turn, these slow-delta oscillations propagate asynchronously across the cortex, inducing a functional disruption of the

connectivity between distinct cortical areas. Moreover, by using a combination of positron emission tomography and functional magnetic resonance imaging (PET/MRI), Akeju et al[12] demonstrated that the main effect of dexmedetomidine-induced LoC was the impairment of the thalamo-cortical functional connectivity.

Connectivity changes within distinct brain regions lead to different depths of anesthesia (DoA). Thus, loss of communication between the thalamus and the cortex is responsible for the beginning of LoC. Subsequently, changes in the cortico-cortical functional connectivity, and in the functioning of several brainstem nuclei (e.g., the ventrolateral preoptic nucleus) as well as in the connectivity between these structures and cerebral cortex are responsible for completing the induction process and, in turn, for maintaining the surgical anesthesia status. During the AE period, mechanisms responsible for LoC and anesthesia maintenance are gradually reversed, whereas other specific awakening mechanisms are activated. These mechanisms encompass several ascending arousal brain pathways responsible for the activation and promotion of the emergence until the RoC. Among the arousal-promoting brain regions involved in the active AE processes, the thalamus has a key role[13]. Alkire et al[14] proved in rats that midline intrathalamic microinfusion of nicotine reversed sevoflurane-induced loss of righting reflex (LORR), an indicative sign of unconsciousness in rodents. Other preclinical investigations, focusing on voltage-gated potassium channels, were performed to assess the role of thalamic central medial nucleus for AE induction[15,16]. However, the thalamic systems are not the sole pathways involved in active AE. Investigations on the dopaminergic (DA)

projections from the substantia nigra (SN) and ventral tegmental area (VTA) of the midbrain to the pedunculo pontine, thalamus, dorsal raphe, locus ceruleus (LC), and laterodorsal tegmental areas, basal forebrain (BF), and lateral hypothalamus)[17,18] suggested the existence of a mesencephalic arousal pathway. It has been shown in animals that the intravenous administration of methylphenidate, or dextroamphetamine which increases the dopaminergic and adrenergic neurotransmission through the reuptake inhibition or the use of a D1 receptor agonist (chloro-APB) restores LORR and increases theta oscillations (decreasing delta- and alfa-power) during inhaled[19,20] or endovenous anesthesia[21]. Furthermore, Taylor et al[22] obtained the same results through a selective stimulation of the VTA dopaminergic neurons, whereas the administration of a D1 antagonist (SCH-23390) attenuated the arousal response. Thus, they called this active transition from the anesthetized state to the awake state “reanimation from general anesthesia”[22].

The hypothalamus is another brain structure involved in the AE mechanisms. The orexinergic neurons are localized in a hypothalamic area around the fiber bundle of fornix. This orexin system (OS) plays a key role in induction of sleep-to-wake transitions, and maintenance of wakefulness[23]. A series of studies proved that it facilitated AE in both intravenous[24], and inhaled general anesthesia[25]. More recently, Zhang et al[26] demonstrated in rats that isoflurane depressed the excitability of orexinergic neurons. Although both orexins (i.e., orexin-A, OXA, and orexin-B, OXB) promoted emergence, OXA played a more significant role (through orexin receptor-1).

Functionally, the OS is related to the locus coeruleus norepinephrine system (LCNE), and the posterior hypothalamic histaminergic tuberomammillary nuclei (TMNHA)[27] which are well-known wake-promoting cell groups of the sleep-wake regulatory network[28], and implicated in the action mechanisms of inhaled anesthesia[29]. In particular, LCNE is functionally connected to the posterior cingulate cortex (PCC), thalamus, and basal ganglia forming the LCNE arousal system, which has been suggested to have an important role in the AE[30]. Orexinergic projections to the hippocampus, and basal ganglia have been also demonstrated[31].

In this complex scenario, there is a functional connection between OS, BF cholinergic structures (i.e., medial septum, vertical limbs of the diagonal band of Broca, nucleus basalis of Meynert, and substantial innominate), and the brainstem ascending reticular arousal system (ARAS). Indeed, the BF has diffuse projections to all parts of the neocortex, basolateral amygdala, and hippocampus, whereas the ARAS has cholinergic cortical projections, and connection with the thalamus, hypothalamus, and the BF region, which in turn modulate the OS (feedback mechanism). The OS contributes to arousal processing by increasing cortical activity due to excitatory projections to wake-promoting cell groups in the posterior hypothalamus, BF, and brainstem. On the other hand, orexin neurons are controlled by positive and negative feedback mechanisms mainly mediated by the hypothalamus and other areas (e.g., perifornical area)[32] and more details on orexin

pathways could be found in literature[33]. Taken together, these data suggest that arousal processes at the end of anesthesia are triggered by structures deep in the brain, rather than being induced within the neocortex.

Electrical activity during recovery from anesthesia

The brain's response to anesthetics recorded with scalp electroencephalogram (EEG) represents the cortical synaptic activity of both excitatory and inhibitory post-synaptic potentials from cortical or thalamic neurons[34]. Apart from this non-invasive EEG modality used in human studies, other approaches such as the electrocorticogram (ECoG, EEG measured directly from the cortical surface), stereoelectroencephalography (SEEG), an EEG performed via depth probes, are used in specific clinical settings (e.g., SEEG in epilepsy) or for experimental investigations in animals. Moreover, neurophysiological changes in the brain under general anesthesia are often studied through a combination of EEG (including hd-EEG methods) with brain activity measures such as functional near-infrared spectroscopy (fNIRS)[35], and neuroimaging modalities, (e.g., functional magnetic resonance imaging, fMRI) [36], or by combining EEG with electrodiagnostic methods, including electromyography and evoked potentials (EP)[37].

Studies on EEG activity during anesthesia induced a significant impetus to research aimed at elucidating the dynamics of anesthesia. Again, technological advances, and mathematical approaches, allowed to apply several brain monitoring devices which

are commonly used in clinical practice. However, explanation of features and clinical utility of DoA monitoring systems is not the scope of this review[38].

Anesthesia-related electrical activity consists of a wide range of EEG patterns, mainly depending on the anesthesia phase (induction, maintenance and emergence), the DoA status, and the type of anesthetics used. Before induction, the awake subject with eyes closed shows a prominent alpha activity (10 Hz) which is maximal over parieto-occipital scalp locations. After inducing anesthesia, EEG pattern shows an increase in beta activity (13-25 Hz) until the LoC[39], whereas during the maintenance phase, different EEG patterns are observed, depending on the DoA level. During a light anesthesia, a decrease in EEG beta band (13-30 Hz) and an increase in both EEG alpha (8-12 Hz) and delta activities (0-4 Hz) may occur. As the DoA state becomes deeper, beta activity decreases, and there is an increase in delta and in alpha frequency band oscillations, with the latter being anteriorly located (“alpha anteriorization”)[40]. A further DoA status features an EEG pattern comprising flat periods interspersed with periods of alpha and beta activity. This characteristic EEG pattern, is known as burst suppression. It can be also recognized in deeper coma status due to various conditions including cerebral anoxia, cancers, drug intoxications, encephalopathies, or hypothermia[41]. The anesthesia-induced burst suppression seems to be associated with a state of cortical hyperexcitability generated by decreased inhibition[42].

As the anesthesia state deepens, EEG shows a progressive stretching between the alpha activities. The amplitudes of the alpha and beta activities progressively decrease, and in turn, the EEG assumes isoelectric form. In this context, the deepest DoA status has been reached[43]. As to the correlation between EEG findings and different anesthetic agents, previous studies showed that this general scheme is particularly applicable for halogenated inhalational anesthetics, and propofol whereas, in contrast, opioids and ketamine usually induce less marked EEG changes. Furthermore, etomidate and barbiturates lead to a rapid shift toward the high voltage delta and theta frequencies[44].

Classically, during emergence it is possible to observe a loss of delta activity, combined with a progressive decrease in frontal alpha power and increased higher frequencies[45]. Moreover, ECoG studies showed that specific findings (i.e., slow oscillation in large-scale functional networks) are maintained during the LoC and RoC phases[46]. However, the canonical EEG sequence during AE can undergo changes. In a fascinating clinical study, Chander et al[47] described different AE patterns. At the beginning of AE, they recognized a pattern characterized by high power of alpha and beta bands (in 95% patients) and termed it as “Slow-Wave Anesthesia” (SWA). The minority of patients had an EEG with a very low spindle and delta power (called “Non Slow-Wave Anesthesia”, NSWA). Interestingly, they also found that EEG patterns between start of emergence and RoC vary, and described four trajectories between the beginning of AE and the RoC. More recently, Liang et al[48] classified emergence EEG patterns in sevoflurane anesthesia. Using

an integrated approach obtained by a multivariate statistical model, they identified four types of emergence EEG patterns. Interestingly, some of these emergence modalities were age-related and could be associated with postoperative mental changes. It can be assumed that the occurrence of different EEG patterns at the emergence reflects the different degrees of influence of brainstem activity on cortical re-connectivity, through the thalamus mediation[13]. This evidence could prove that AE modulation can be mostly obtained by controlling brainstem activity (e.g., by opioids). Although we adopted a general descriptive scheme (i.e., anesthesia-induced EEG changes at the emergence), it is important to underline that because of the distinct mechanisms of action, different anesthetics may induce different types of EEG dynamics, also in the AE phase. Recent studies are increasingly characterizing these profiles[49], especially with regard to dexmedetomidine[50].

CLINICAL IMPLICATIONS

A better understanding of AE mechanisms has significant clinical implications, such as improving the quality of recovery of patients following surgery. It has been proved that the EEG modality at the emergence affected the residual level of sedation and post-operative pain[47]. Thus, in a hypothetical scenario, it could be possible to modulate the path of emergence, choosing the one which correlates with the desired target. The possibility to increase the predictability of the time of emergence may help prevent delayed emergence - defined as the failure to regain consciousness 30-60 min after general anesthesia[51] - and other more frequent AE complications, such as ED, and respiratory complications. This is a significant issue

as delayed emergence was associated with a longer postoperative hospital stay[52], whereas ED in children may lead to physical harm in the children and distress in patients, parents and staff. Moreover, although usually self-limiting, it can last up to 48 h, and children who manifested ED are more likely to suffer from new-onset postoperative maladaptive behavioral changes[53]. Again, ED in adults can lead to serious complications, such as self-extubation, accidental removal of catheters and injury[54].

Although about 20% of accidental awareness with recall during general anesthesia (AAWR) occur at the AE, and 90% of these cases are potentially preventable (e.g., through the use of neuromuscular monitoring)[55], in very rare AAWR cases there is no readily identifiable cause[56]. A more precise AE management can help avoid these unexpected awakening events, which are often associated with severe psychological consequences, such as post-traumatic stress disorder (PTSD).

NEUROPHYSIOLOGICAL RESPONSE DURING EMERGENCE IN NEUROSURGICAL PATIENTS

Several physiological changes take place during the emergence from anaesthesia including metabolic variations and those affecting brain homeostasis. Even with slightly normal PaCO₂ levels, bicarbonate levels in the cerebrospinal fluid (CSF) may decrease significantly.⁷ Therefore, consequent pH reduction in brain perivascular areas will lead to vasodilation and hyperemia.⁷ Apparently, these events occur regardless of the anesthetic agent used during maintenance. Bruder et al.

reported a significant increment of 60% from baseline in CBF velocity during extubation and within the first hour after neurosurgery, with no relation found between these values and the surgery or anesthesia techniques.⁸ Increased catecholamine blood levels have been reported after neurological surgery.^{7,8} However, this condition by itself may interfere with the CBF only in the presence of a defective blood–brain barrier or when autoregulation is compromised.⁸ Different options are available to treat catecholamine hemodynamic effects such as β -blocker use (e.g., esmolol)^{9,10} and hypothermia prevention.¹¹ On the other hand, sympathetic activation may play a crucial role on the central nervous system (CNS) responses during emergence from anesthesia. Reuptake inhibition of dopamine and norepinephrine by methylphenidate administration will trigger several mechanisms within the CNS leading to a faster recovery after isoflurane and propofol exposure.^{12,13} Surgery and anesthesia may also increase the incidence of emesis during the emergence. The “emesis center” includes the area postrema (AP), nucleus tractus solitarius, and the dorsal motor nucleus of the vagus nerve. No less than 17 neurotransmitters exert their action on this center throughout the interaction with several receptors such as dopamine, substance P/neurokinin-1, cannabinoid, histamine, among others.¹⁴ The aforementioned responses may be generated during extubation as a result of the autonomic nervous system activation.

SPECIFIC PERIOPERATIVE CONSIDERATIONS

Diagnosis of potential postoperative complications may be delayed due to a slow return to consciousness mak-

ing neurological examination difficult to perform after neurosurgery. Postanesthesia arousal is a variable considered

when assessing anesthesia quality.^{15,16} Preoperative neurologic status, location and size of the lesion, and anesthesia

technique are some of the variables interfering with the early postoperative recovery of cognition, hemodynamics,

and nociception during emergence.

Surgical Site and Lesion Location

Brain herniation, ischemia, and poor surgical field are the expected consequences of increased intracranial volume.

These events have been associated with delayed arousal after intracranial surgery.¹⁰

Predictive factors for delayed

postsurgical emergence are the following: mass effect of space-occupying lesion (over 30 mm size), cerebral struc-

tures shifting from midline >3 mm with perilesional edema, and prolonged retraction pressure needed to expose the

surgical field during tumor resection.¹⁰

Anesthetic Techniques

Definitive criteria for quality of recovery related to the anesthesia technique during neurosurgical procedures

have not been established.¹⁵ However, a targeted and neurological evaluation is performed at the end of surgery to

assess outcomes.¹⁷

The Short Orientation Memory Concentration Test (SOMCT) and the Aldrete score are commonly used when

comparing the time and quality of recovery of patients undergoing supratentorial craniotomy, either under balanced

or TIVA technique.^{18,19}

VII. NEUROSURGERY-SPECIFIC PERIOPERATIVE CONSIDERATIONS 249

TIVA based on propofol–remifentanyl has shown slightly shorter extubation time, faster return to consciousness, and faster recovery in comparison with balanced anesthesia.^{17,20} However, most of the studies have demonstrated no statistical significance in quality of recovery among patients either when TIVA or balanced anesthesia was performed.^{5,18,21–24}

The NeuroMorfeo Study was carried out in 411 patients reporting no difference in time after extubation to achieve an Aldrete score ≥ 9 between both balanced and TIVA groups. Hemodynamics and brain surgical conditions were also similar among groups. Nevertheless, a reduced endocrine response to surgical stress was linked to propofol/remifentanyl combination.²⁴

Balanced Anesthesia

Desflurane provides shorter extubation and recovery time than sevoflurane in patients undergoing craniotomy under balanced anesthesia.^{25,26} Magni et al. compared the effects of sevoflurane (1.5–2%) and desflurane (6–7%) on emergence analyzing the data collected from 120 neurosurgical patients. No significant difference was found regarding the time for emergence (12.2 ± 4.9 min versus 10.8 ± 7.2 min), recorded as the time when eye opening occurred since the inhaled agent administration was suspended. On the other hand, the sevoflurane group needed more time for tracheal extubation in contrast to the desflurane group (18.2 ± 2.3 min versus 11.3 ± 3.9 min). Similarly, the time of recovery (defined in this study as the time that patients' consciousness allowed them to repeat their name and date of birth) was longer in the sevoflurane group (12.4 ± 7.7 min versus 1.3 ± 3.9 min).²⁵ The characteristic of the surgical field, such as state of the brain tissue and the intracranial pressure (ICP) and postoperative cognitive function are also comparable between both inhaled anesthetics during supratentorial surgeries.²⁷ Cognitive impairment commonly occurs in both groups within the first 15 min after extubation²⁵ or after Aldrete score was ≥ 9 , usually returning to baseline during the next 30 min.²⁶ Moreover, when compared with opioids such as fentanyl, alfentanil, and sufentanil in combination with isoflurane showed no clinical relevance regarding the time for obtaining a satisfactory neurological evaluation after surgery.²⁸

Total Intravenous Anesthesia

Despite the advantages of propofol use in neurosurgery such as reduction of cerebral metabolic rate of oxygen and ICP, increase of cerebral perfusion pressure (CPP), and antiemetic effect,^{17,29–32} adverse events like shivering, high blood pressure, and

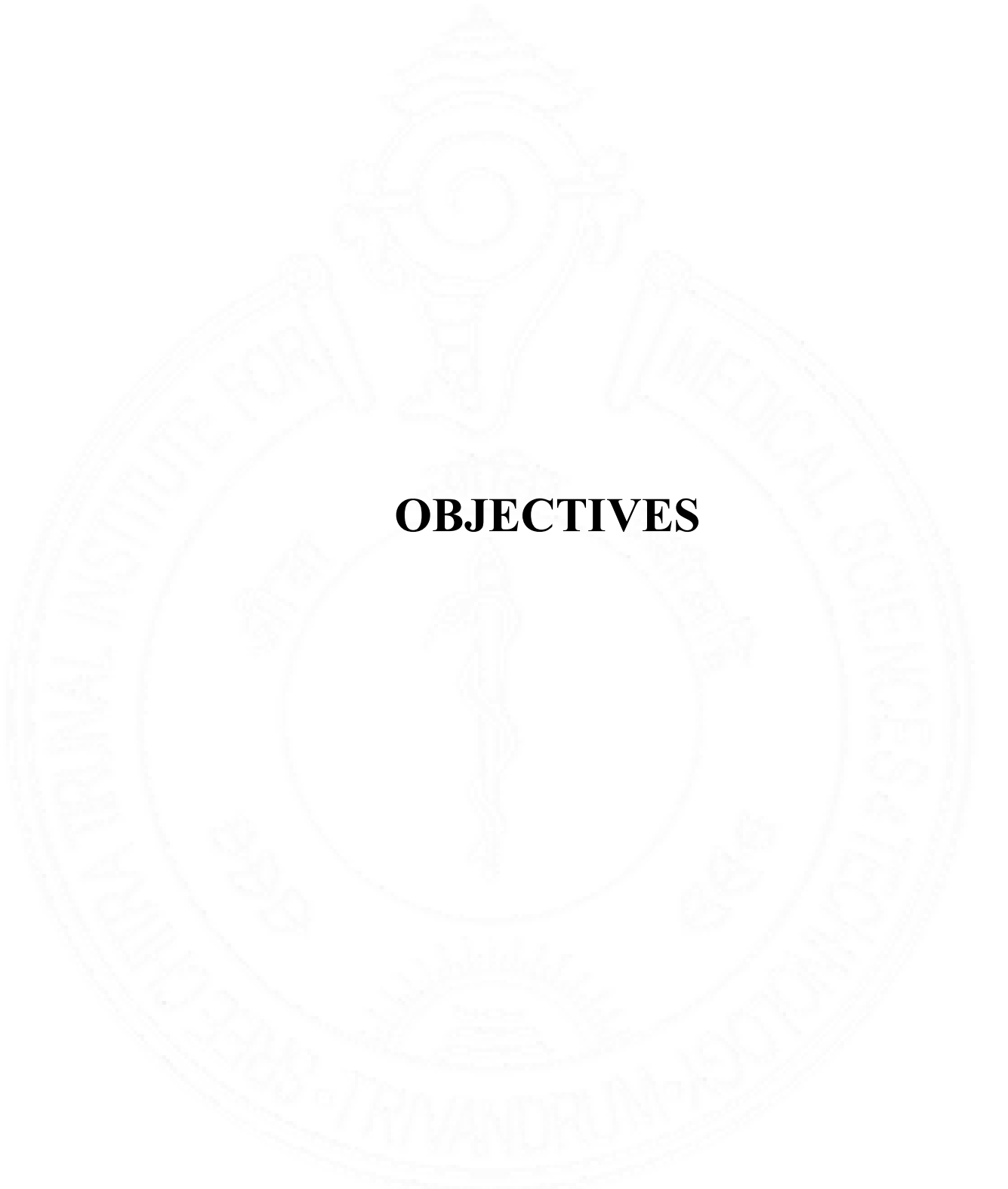
postoperative nausea and vomiting (PONV) are not uncommon.⁴ The effects and outcomes of several combinations of opioids and propofol infusions have been compared during neurosurgery with different results. Gerlach et al. compared propofol/remifentanyl versus propofol/sufentanyl in supratentorial surgeries and reported a reduced time for extubation in the remifentanyl group (6.4 min vs. 14.3 min).³³

When remifentanyl/propofol combination was used, SOMCT and Rancho Los Amigos Scale scores are comparable to baseline sooner than the interval of time reported by sufentanyl/propofol group.¹⁹ Nevertheless, Djian et al. showed similar results among groups regarding extubation time and reported an increase in costs in the remifentanyl group when compared to the sufentanyl group.³⁴

On the other hand, remifentanyl is characterized by a faster onset in reducing cardiovascular responses during intubation when compared with fentanyl. However, hemodynamic parameters, ICP, and CPP levels are similar during the maintenance of anesthesia with both, remifentanyl and fentanyl, whereas naloxone administration after neurosurgery is importantly increased in patients who received fentanyl.³⁵ Moreover, remifentanyl/propofol seems to be a common option for transsphenoidal procedures as it may offer a reduced incidence of postoperative coughing during and after extubation by providing an ideal emergence.³⁶ In fact, these studies provide more evidence on the convenience of using opioid drips in neuroanesthesia as discontinuation at an appropriate time will result in a shorter extubation and recovery.

Anesthetic Technique and Recovery of Cognitive Function

Recovery of cognitive functions after surgery has become one of the major concerns among neuroanesthesiologists and also an important parameter when comparing different anesthetic techniques in neurosurgical patients.³⁷ In fact, a connection between the pathogenesis of neurodegenerative diseases and the development of postoperative cognitive dysfunction has been described.³⁷



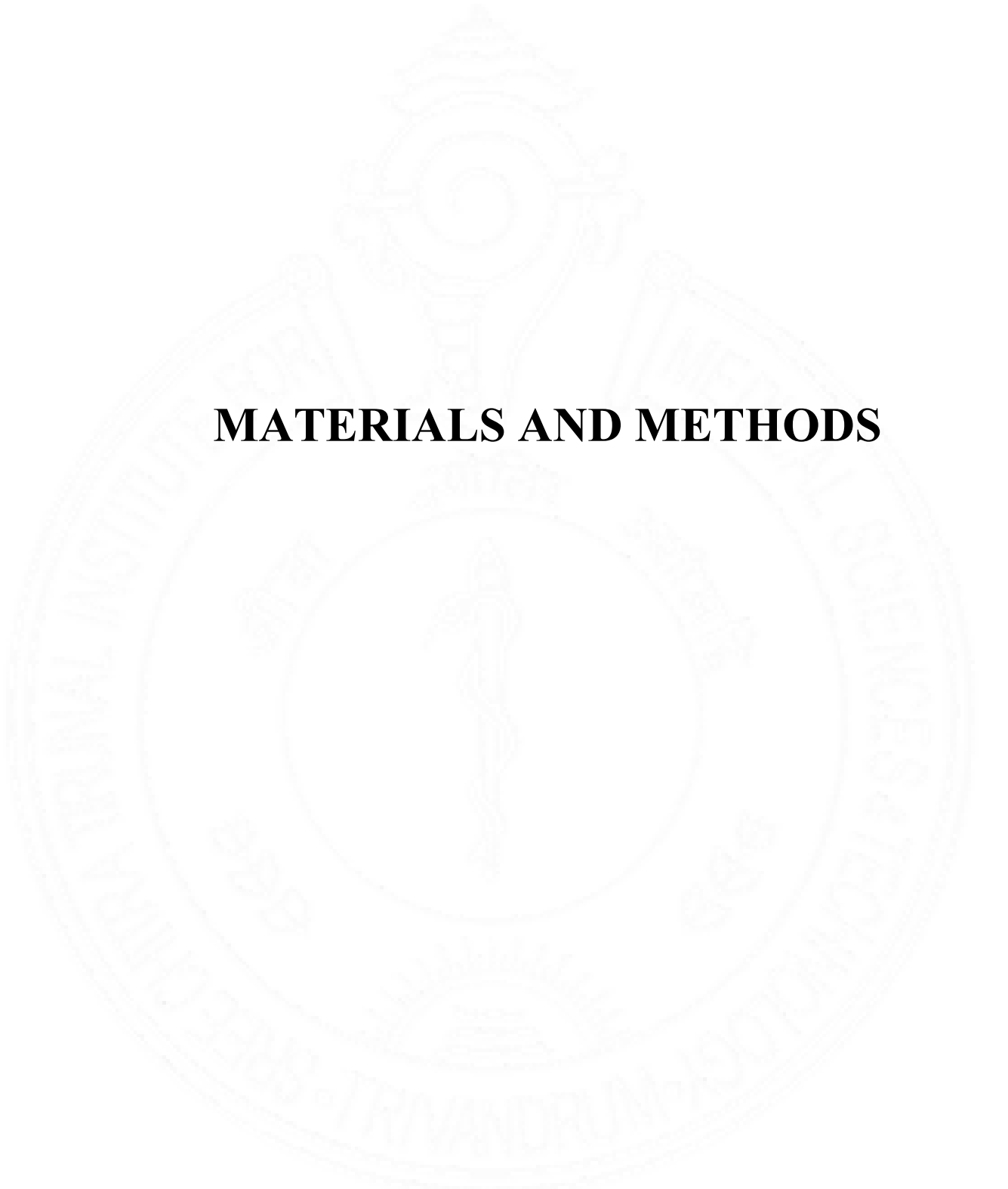
OBJECTIVES

Hypothesis:

The changes in pupillary reflexes measured using automated pupillometry seen during emergence of patients from general anaesthesia who undergo supratentorial craniotomies correlates with frontal EEG changes and Bispectral index values.

Objective:

- Assessment of correlation of change in pupillometric indices (pupillary size, constriction velocity, latency time and dilatational velocity) to changes in BIS during emergence from general anaesthesia
- Assessment of correlation of change in pupillometric indices (pupillary size, constriction velocity, latency time and dilatational velocity) to changes to spectral edge frequency obtained from frontal EEG during emergence from general anaesthesia.



MATERIALS AND METHODS

3 MATERIALS AND METHODS

This is a prospective observational study designed to evaluate the changes in pupillometric indices during emergence from general anaesthesia in patients undergoing elective supratentorial neurosurgical procedures and its correlation with Bispectral index values..

Setting: Neurosurgical operation theatre (NSOT) at Sree Chitra Tirunal Institute of Medical Sciences & Technology (SCTIMST), Thiruvananthapuram, a specialized tertiary care referral center.

Institutional Ethics Committee Approval: This study was approved by our Institutional Ethics Committee (SCT/IEC/1804/JANUARY/2022)

Study period: Patients were enrolled from March 2024 to November, 2024 for the study.

Study Design: Prospective observational case study. The total number of participants are s.

The patients for the study were selected from elective neurosurgical operation theatre list and recruited after fulfilling the following inclusion and exclusion criteria. Informed written consent was obtained from those who fulfilled the recruitment criteria and those willing for the study were included in the study.

Inclusion criteria:

- American Society of Anesthesiologist (ASA) physical status class I and II
- Both gender
- Age 18-65 years , undergoing elective craniotomy for supratentorial lesions.
- Patient's or legal heir's consent

Exclusion criteria

ASA class III, IV PATIENTS

- Age < 18 years, > 65 years
- Severe or uncompensated cardiovascular, renal, hepatic or endocrine disease
- Pregnancy, postpartum, lactating females
- Patients with preoperative cognitive dysfunction
- Preoperative GCS less than 15
- Patients with preoperative anisocoria
- Patients with history of cataract surgery, glaucoma, ocular trauma, tumours affecting optic and oculomotor pathway
- Refusal to consent by patient or legal heir
- Patients who are intubated and on mechanical ventilation
- Emergency surgery

Study protocol

After IEC approval and informed patient consent, patient will be recruited for the study

- Patients will be recruited from the wards of neurosurgery department
- The patient history and clinical findings will be collected from the time of admission.
- The principal investigator will see the patients and screen for the inclusion criteria and exclusion criteria.
- After detailed pre-anaesthetic evaluation, on the day prior to surgery, patient would be kept fasting for 6 hours for solids and 2 hours for clear liquids.
- On the day of intervention, patient will be shifted to operation theatre. Safety checklist will be filled as per protocol.
- In the procedure room, patient will be placed in supine position and a wide bore intravenous cannula will be secured under local anaesthesia and maintenance intravenous fluid will be started.
- Standard ASA monitors- electrocardiogram, oxygen saturation, non-invasive blood pressure will be placed. In addition, BIS monitor to assess depth of anaesthesia also will be placed.
- Baseline pupillometric indices will be recorded prior to general anaesthesia using Neurolight pupillometer by IDMED and patients with abnormal baseline neurological pupillary index of less than 3 will be excluded. Baseline pupillometric indices viz. pupillary size, constriction velocity, latency time and dilatational velocity will be recorded. (Time point T0)

- Baseline frontal EEG and BIS values will also be recorded using Medtronic Bispectral Index™ (BIS™) Monitoring System

- General anaesthesia will be induced with propofol and vecuronium.

Maintenance of anaesthesia will be maintained using sevoflurane titrated to BIS value of 40 to 60 and intraoperative analgesia shall be maintained using scalp block using 0.25% bupivacaine and intraoperative infusion of fentanyl at 1 microgram/kg/hr infusion.

- Intraoperative blood loss, total fentanyl usage, intraoperative brain relaxation score and hemodynamics will be recorded.

- At the point of termination of anaesthetics pupillometric indices, Bis values, spectral edge frequency, and hemodynamic indices noted. (Time point T1)

- Pupillometric indices will be repeated when Bis value increases above 60. (Time point T2)

- Pupillometric indices, BIS values and SEF will also be noted at point of first clinical response (Time point T3) and at point of extubation (Time point T4)

- Time from termination of anaesthetics to increase of BIS to 80 and time of eye opening to verbal command will be noted.

Data collection: The following observations are manually entered into the study proforma

1. Baseline Heart rate, SBP, DBP, MAP and oxygen saturation (SpO₂) were recorded on day prior to surgery

2. QPi, PD, CV and LAT prior to induction of anaesthesia, end of surgery, after BIS increases above 60, at the point of first clinical response, and at the point of extubation.
3. SBP, DBP, MAP, SpO₂, PaCO₂ prior to induction of anaesthesia, end of surgery, after BIS increases above 60, at the point of first clinical response, and at the point of extubation.
4. Time taken from termination of anaesthetics to BIS > 60 and QPI >3 also noted.

STATISTICS

Sample size calculation

This will be a prospective observational study. We plan to conduct a pilot study with a total sample size of 40, with a subset of 5 participants specifically allocated to account for any potential dropouts. There are no previous studies of similar model studying the changes in pupillometric indices during emergence from anaesthesia.

Data analysis

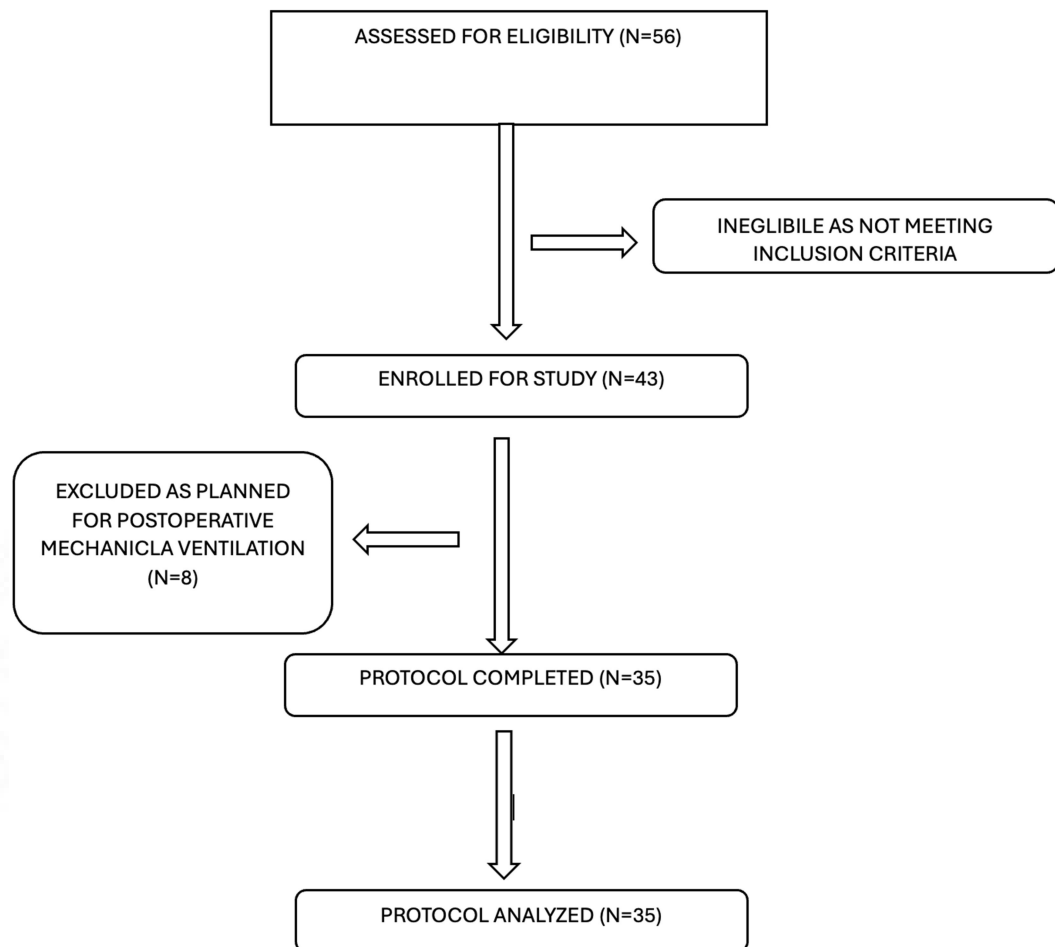
Data is manually entered into the proforma by the investigators. It will not be analysed to understand, gender, caste, class, ethnicity and race difference. All statistical analyses were performed using IBM SPSS Statistics software version 29.0 for Macintosh (Armonk, NY: IBM Corp). Descriptive data were expressed in frequency, percentage, mean and standard deviation. Kolmogorov Smirnov was done to check whether the distribution of data was normal. One-way repeated measures variance analysis (ANOVA) was used for the inter-comparison of relative changes in PD, QPi, CV and LAT as well as BIS and SEF values and hemodynamics with different time points. Significance was accepted when probability value was ≤ 0.05 level with post hoc Bonferroni corrections for minimizing type I error for multiple comparisons. For data with non-normal distribution related-samples Friedman's two-way analysis of Variance by ranks was done. A p value of ≤ 0.05 was considered as significant after the significance value has been adjusted by the

Bonferroni correction for multiple tests. Correlation between change in pupillometric indices (pupillary size, constriction velocity, dilatational velocity, latency time, neurological pupil index) to change in BIS values between different time points and between change in pupillometric indices (pupillary size, constriction velocity, dilatational velocity, latency time, neurological pupil index) to change in spectral edge frequency values between different time points was assessed using Spearman correlation analysis.

4 RESULTS

A total of 56 patients were assessed for eligibility, with 43 eventually enrolled in the study; 8 subjects were excluded due to intraoperative complications that required postoperative ventilation, resulting in a successful completion of the study with 35 patients. (Figure 1). The mean age was 44.1 ± 13.73 years, and the majority of patients were female (54.2%), with 62.86% classified as ASA grade 1 and 37.14% as ASA II.

Figure : Flow chart depicting the enrolment, study inclusion, and data analysis



The mean heart rate at T0 was found to be 75.2 ± 11.4 /minute, which reduced to 65.81 ± 7.23 /minute at T1 and 79.94 ± 6.15 /minute at T2, 90 ± 8.37 /minute at T3, 95.17 ± 8.53 /minute at T4 which was statistically significant ($p\text{-value} < 0.05$). The mean arterial pressure decreased from 111 ± 7.33 at T0 to 99.52 ± 6.68 at T1 and later increased to 97.44 ± 6.91 at T2, 99.1 ± 6.48 at T3 and 119. This change was also statistically significant with $p\text{-value} < 0.001$. The analysis of SPO₂ and PaCO₂ values at the different time points did not reveal any difference from time points T1 to T4, as shown in Table 1 ($p\text{-value} > 0.05$).

Table 1: Table showing demographic data of subjects

AGE	BMI	ASA GRADE	GENDER
44.1±13.73	23.9±3.33	ASA 1: 22 (62.86%) ASA 2: 13 (37.14%)	Male – 16 (45.71%) Female – 19 (54.2%)

The mean heart rate at T0 was found to be 75.2 ± 11.4 /minute, which reduced to 65.81 ± 7.23 /minute at T1 and 79.94 ± 6.15 /minute at T2, 90 ± 8.37 /minute at T3, 95.17 ± 8.53 /minute at T4 which was statistically significant (p-value < 0.05). The mean arterial pressure decreased from 111 ± 7.33 at T0 to 99.52 ± 6.68 at T1 and later increased to 97.44 ± 6.91 at T2, 99.1 ± 6.48 at T3 and 119. This change was also statistically significant with p-value < 0.001. The analysis of SPO2 and PaCO2 values at the different time points did not reveal any difference from time points T1 to T4, as shown in Table 1 (p-value> 0.05).

Table 2: Table depicting haemodynamic variables of the subject at various time points

		T0	T1	T2	T3	T4	P-value
HR	MEAN	75.17	66.81	79.94	90.00	95.17	<0.01
	SD	11.40	7.23	6.15	8.37	8.53	
SBP	MEAN	131.69	114.47	128.50	137.72	154.25	<0.01
	SD	15.42	9.61	7.89	10.43	13.06	
DBP	MEAN	77.89	67.25	74.83	80.36	87.78	<0.01
	SD	10.91	7.48	5.85	5.71	4.13	
SP02	MEAN	99.19	99.19	99.28	98.97	99.00	0.159
	SD	0.75	0.79	0.78	0.77	0.79	
PaCO2	MEAN	36.97	36.72	37.64	37.22	36.36	0.336
	SD	2.97	2.72	3.33	2.09	2.74	

The repeated measures ANOVA analysis of pupillary diameter (PD), Quantitative Pupillometry Index (QPi), and constriction velocity (CV) showed a significant increase across the time periods, while a reduction in latency was seen across T1 to T4 with a significance level of less than 0.01 (Table 2). As expected, the changes in the BIS values and spectral edge frequency during emergence were also significant across the time points. (Table 2).

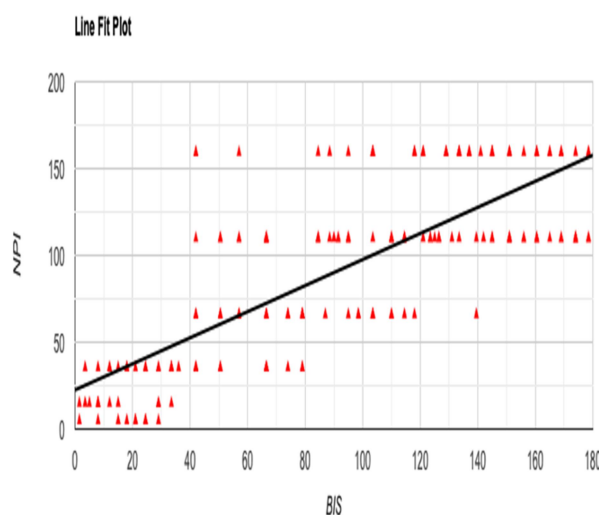
Table 3: Table showing pupillometric indices and processed EEG data at various time points

		T0	T1	T2	T3	T4	
PD	MEAN	4.53	2.56	2.74	3.34	4.50	<0.01
	SD	0.87	0.43	0.48	0.37	0.31	
NPI	MEAN	2.94	1.38	1.90	2.32	2.68	<0.01
	SD	0.36	0.21	0.32	0.23	0.23	
CV	MEAN	4.37	1.83	2.77	3.35	3.96	<0.01
	SD	0.33	0.38	0.39	0.32	0.37	
LAT	MEAN	0.26	0.36	0.30	0.26	0.25	<0.01
	SD	0.03	0.04	0.04	0.03	0.03	
BIS	MEAN	95.50	47.39	62.25	71.17	83.36	<0.01
	SD	2.27	4.70	1.75	6.80	5.22	
SEF	MEAN	25.14	9.25	13.83	19.11	23.97	<0.01
	SD	3.28	1.46	1.52	2.75	2.24	

There was a large positive relationship between BIS and QPi ($r(180) = .77, p < .001$) and between BIS and CV ($r(180) = .86, p < .001$). Additionally, a significant large negative correlation was observed between BIS and latency ($r(180) = -.62, p < .001$). Furthermore, SEF showed significant large positive relationships with QPi ($r(180) = .78, p < .001$) and CV ($r(180) = .85, p < .001$). The negative correlation between SEF and latency was also significant ($r(180) = -.62, p < .001$)

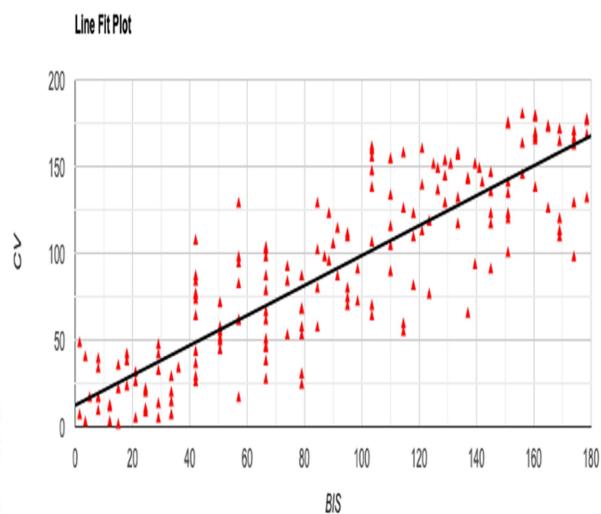
The time taken from the termination of anaesthetics to an increase in $QPi > 3$ (10.25 ± 2.03 minutes) was significantly shorter than the time required for the BIS to exceed 60 (11.94 ± 2.73 minutes), with a p-value < 0.01 .

Figure 2: Figure showing correlation between QPI and BIS



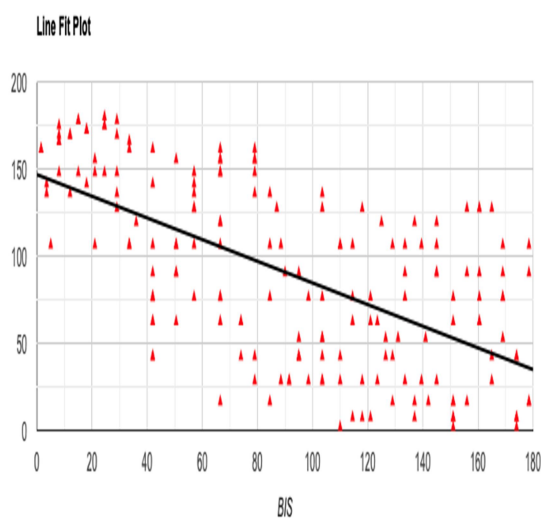
Parameter	Value
Spearman's rank correlation coefficient (r_s)	0.7719
r^2	0.5958
P-value	<0.01
Covariance	2036.5475
Sample size (n)	180
Statistic	16.1971

Figure 3: Figure showing correlation between CV and BIS



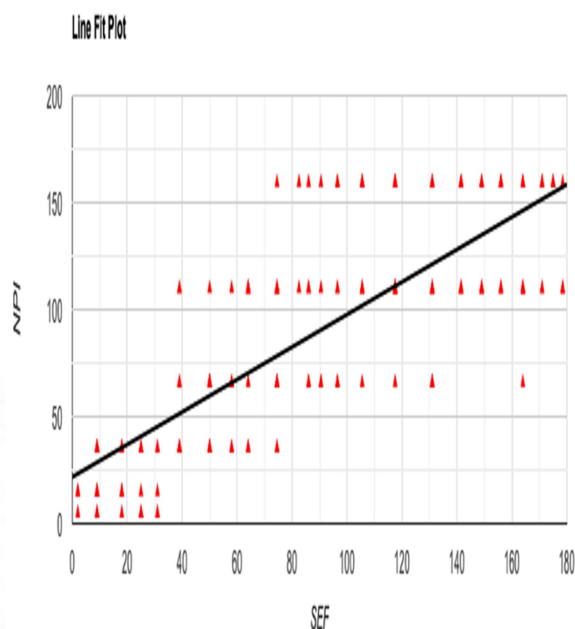
Parameter	Value
Spearman's rank correlation coefficient (r_s)	0.8619
r^2	0.7428
P-value	<0.01
Covariance	2338.514
Sample size (n)	180
Statistic	22.6726

Figure 3: Figure showing correlation between latency and BIS



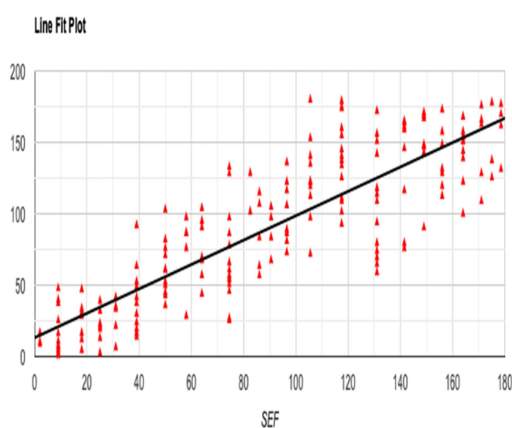
Parameter	Value
Spearman's rank correlation coefficient (r_s)	-0.6221
r^2	0.387
P-value	<0.01
Covariance	-1684.3478
Sample size (n)	180
Statistic	-10.601

Figure 4: Figure showing correlation between QPI and SEF



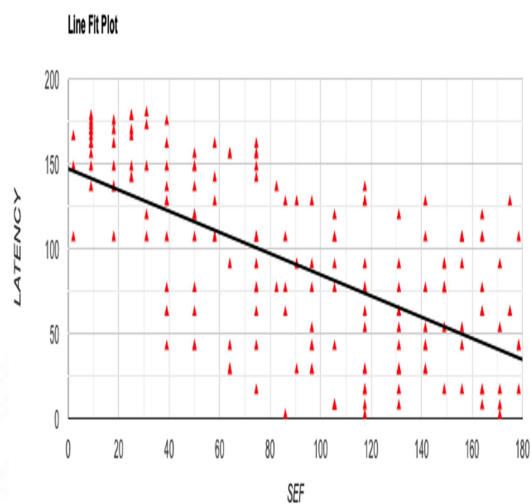
Parameter	Value
Spearman's rank correlation coefficient (r_s)	0.7797
r^2	0.608
P-value	<0.01
Covariance	2055.4651
Sample size (n)	180
Statistic	16.6141

Figure 5: Figure showing correlation between CV and SEF



Parameter	Value
Spearman's rank correlation coefficient (r_s)	0.8527
r^2	0.7271
P-value	<0.01
Covariance	2311.5824
Sample size (n)	180
Statistic	21.7747

Figure 2: Figure showing correlation between latency and SEF



Parameter	Value
Spearman's rank correlation coefficient (r_s)	-0.6243
r^2	0.3897
P-value	0.069
Covariance	-1688.7528
Sample size (n)	180
Statistic	-10.6616



DISCUSSION

5 DISCUSSION

Our research presents the first comprehensive analysis comparing pupillometry and processed electroencephalography (EEG) as methods for evaluating the emergence from anaesthesia in patients undergoing neurosurgery. This study aims to provide valuable insights into the effectiveness of these two assessment techniques in monitoring recovery responses in a sensitive surgical population.

Our study revealed a statistically significant increase in pupillary size, pupil constriction index (QPI), and constriction velocity from the time of anesthetic termination to the point of extubation, along with a significant reduction in latency time. Kum et al. initially observed mydriasis during the emergence phase from isoflurane anesthesia.(9) Sabourdin et al. demonstrated that cetirizine and propofol had a dose-dependent effect on pupillary diameter, showing a reduction in diameter with increasing doses of propofol.(10) Similarly, Haddock et al. reported a decrease in pupillary diameter and constriction velocity, as well as an increase in latency during higher levels of propofol sedation.(11) However, studies examining changes in pupillometric indices during emergence from anesthesia in humans are lacking.

Our analysis demonstrated a significant and substantial positive relationship between the Bispectral Index (BIS) and QPI ($r(180) = .77, p < .001$). Additionally, we identified a significant and strong positive correlation between BIS and the CV($r(180) = .86, p < .001$). In contrast, there was a notable large negative correlation between BIS and latency ($r(180) = -.62, p < .001$). Rouche et al. investigated the effects of sedation depth on pupillometry indices in mechanically

ventilated patients.(12) They compared the maximum contraction velocity of the pupil (V_{max}) and variations in pupil diameter (PD) across three groups categorized by sedation levels, as indicated by the BIS. The groups were classified as follows: heavy sedation ($BIS < 40$), acceptable sedation ($BIS 40-60$), and light sedation ($BIS > 60$). The findings revealed a significant difference in V_{max} between the heavily sedated group and the acceptable sedation group ($P < .0001$). Furthermore, there was a significant difference in the variation of PD ($P < .0001$) between these two groups. Similarly, significant distinctions were observed in both V_{max} ($P < .0001$) and the variation in PD ($P < .0001$) when comparing the heavy sedation group to the light sedation group. However, Shirozu et al. did not find any correlation between Neurological pupillary index (NPI) and BIS values in thirty-five patients scheduled for breast or thyroid surgery under general anaesthesia.(13)

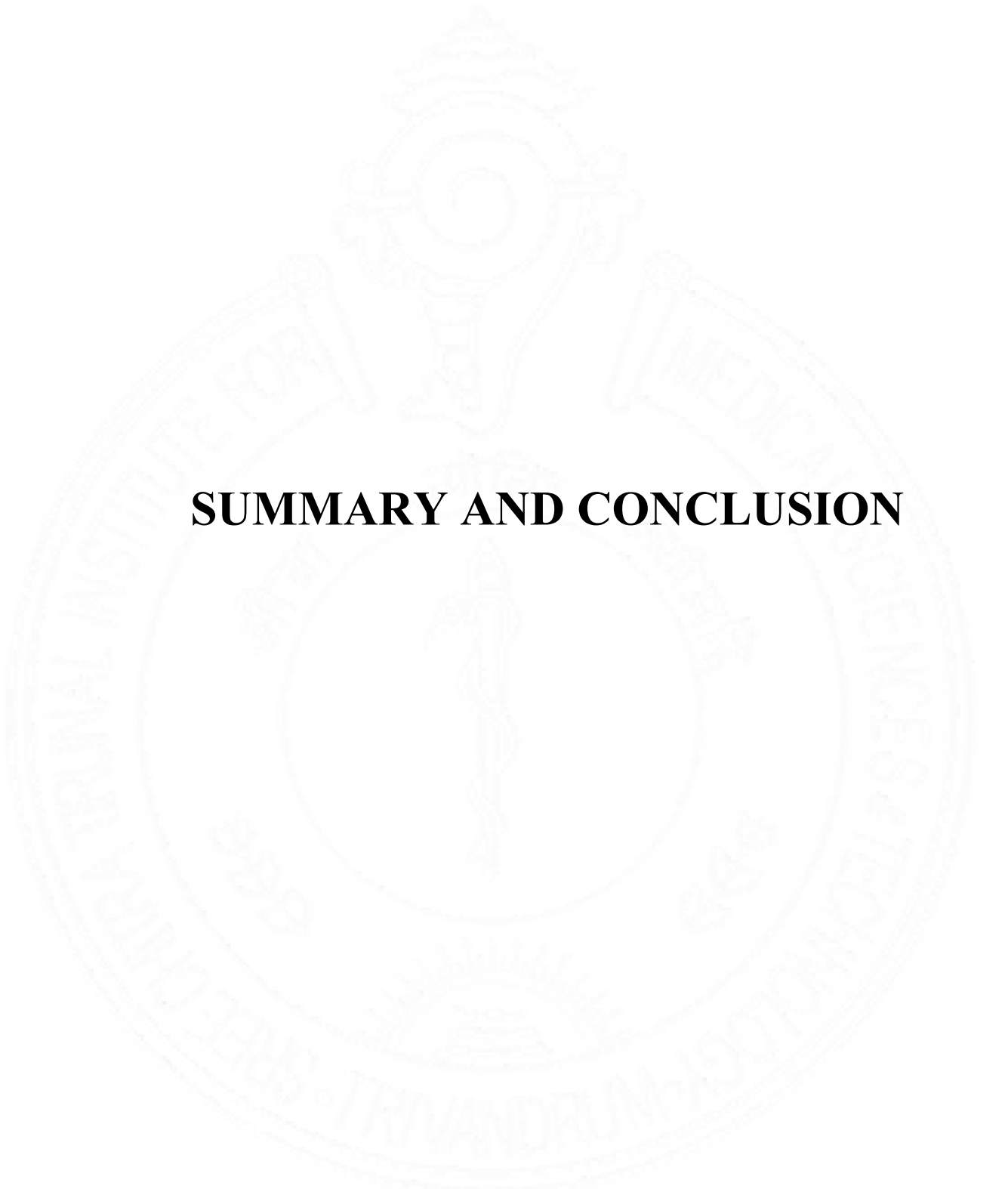
The correlation analysis of pupillary indices and SEF in our study population revealed a significant large positive relationship between SEF and the NPI ($r(180) = .78, p < .001$) and between SEF and CV ($r(180) = .85, p < .001$). Additionally, SEF demonstrated a significant negative correlation with latency ($r(180) = -.62, p < .001$). This was in accordance with the findings of Lim Shi, who found strong correlations between percentage pupillary light reflex (%PLR) and RASS ($Rho=0.635$) and between %PLR and SEF ($R=0.641$) in critically ill patients.(14)

The use of BIS in the quantitative monitoring of emergence from general anaesthesia remains controversial because of the false elevation by EMG activity.(15) SEF, which is less influenced by EMG, has been used to assess the level of hypnosis during general anaesthesia.(16,17) The high positive correlation between

SEF and RASS shows that SEF can differentiate between different depths of anaesthesia although the reliable interval is lacking.(14) Among the correlations established, the best relationship was between CV and BIS.

We have clearly established that the changes in QPi well precede the changes in electrocorticography in our subjects. This is in clear accordance with the findings of Kum et al. who concluded that pupil diameter precedes electrophysiological change of the brain during a transitional state of anaesthesia. Observing pupil diameter enables watching out transitional state of anesthesia without recording electrophysiological activation during surgery.(9) There is extensive evidence of functional relationships between Locus Coeruleus(LC) activity and pupil dilation. In humans, fMRI studies combined with pupillometry measures have shown that LC activity increases together with pupil size during behavioral tasks and in resting.(18) Another fMRI study, conducted on humans performing an oddball task, pupil size changes have been described to covary with blood-oxygen-level-dependent (BOLD) signal localized to LC.(19) Moreover, the electrical stimulation of LC in anaesthetized and awake animals evokes pupil dilation.(20–22) These data support the idea of a direct coupling between the LC and pupil diameter. The LC could act directly on neurons in the Edinger-Westphal nucleus, with nor-epinephrine binding the inhibitory α_2 -adrenergic receptors.(23) However, the existence of a direct pathway is still controversial.(24) The activation of LC has also been observed during emergence from anaesthesia.(25,26) This activation of the locus coeruleus can result in subsequent pupillary dilation during emergence, explaining why changes in pupil size precede electrophysiological changes in the cortex during this process.

It is essential to address certain limitations in our study. Firstly, this was a pilot study with a limited sample size, suggesting that the findings may not be generalizable. Various conditions, such as indoor light levels, the device used for pupillary light reflex (PLR) assessment, and the dosage of opioids and hypnotics administered, could independently influence PLR by affecting pupil size.(13) It is well established that Opioid drugs inhibit PRD after nociceptive stimulation by blocking nerve conduction between brainstem inhibitory neurons and the Edinger-Westphal nucleus. (27) Additionally, an assessment of pain was not performed in this study. Since Nociceptive stimulation inhibits the Edinger-Westphal nucleus to dilate the pupillary, the degree of dilation is positively correlated with the intensity of the nociceptive stimulation.(27)



SUMMARY AND CONCLUSION

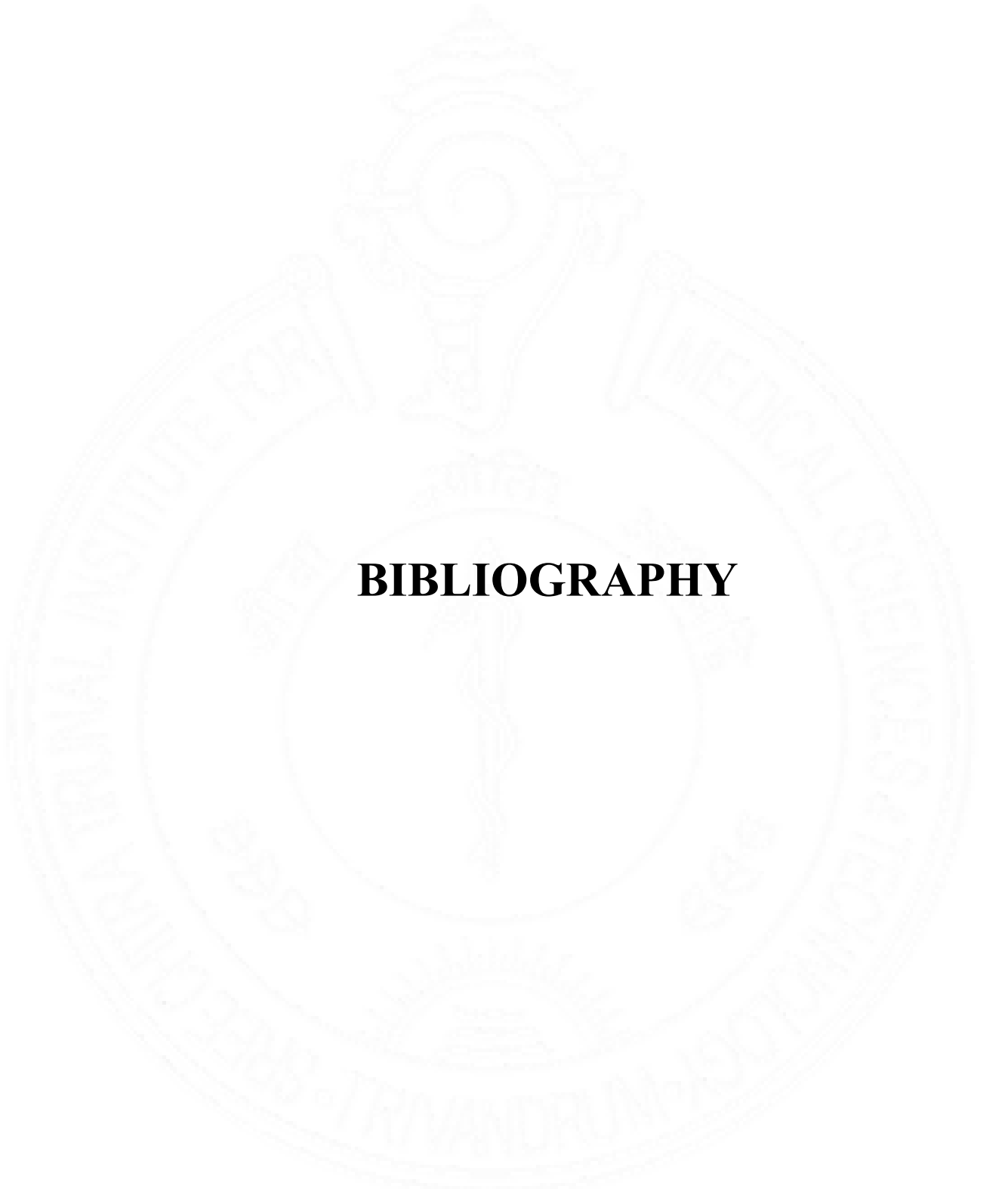
6 SUMMARY AND CONCLUSION

This study was conducted with a prospective observational design to assess the change in pupillometric indices during emergence from anaesthesia in comparison to BIS in patients undergoing supratentorial surgery. Our hypothesis was that The changes in pupillary reflexes measured using automated pupillometry seen during emergence of patients from general anaesthesia who undergo supratentorial craniotomies correlates with frontal EEG changes and Bispectral index values. The study assessed the middle cerebral artery blood velocities and cerebral autoregulation through transcranial Doppler (TCD) and measured intracranial pressure through optic nerve sheath diameter (ONSD) before and after the initiation of SNP treatment for hypertension control in 35 patients who underwent elective posterior fossa surgery. The parametric data was analyzed using repeated measures ANOVA with Bonferroni correction while the non-parametric data was analyzed using Friedman's two way analysis of variance. We also The analysis of our data revealed the following:

1. significant increase in pupillary diameter, constriction velocity, QPI, and significant reduction in latency across time points
2. significant large positive relationship between BIS and NPI, ($r(180) = .77, p < .001$), significant large positive relationship between BIS and CV, ($r(180) = .86, p < .001$)
3. Significant large negative correlation between BIS and latency ($r(180) = -.62, p < .001$)

4. Significant large positive relationship between SEF and NPI, ($r(180) = .78, p < .001$), SEF and CV, ($r(180) = .85, p < .001$)
5. Significant large negative correlation between SEF and latency ($r(180) = -.62, p < .001$)
6. The pupillometric changes preceded the changes in BIS

Based on our findings we conclude that assessment of pupillary light reflex by automated pupillometry may provide a qualitative indication for emergence from anaesthesia in patients undergoing supratentorial surgery. Its usefulness, particularly when used in combination with other depth of anaesthesia monitors deserves further study.



BIBLIOGRAPHY

7. BIBLIOGRAPHY

1. Lewelt W, Hummel R, Littlewood K. Recovery from anesthesia and cerebral blood flow velocity. *Anesth Analg*. 1992;74(186).
2. Forster A, Horn K, Marshall LF, Shapiro HM. Anesthetic effects on blood-brain barrier function during acute arterial hypertension. *Anesthesiology*. 1978;49(1):26–30.
3. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. *Anesthesiology*. 2000;93(1):48–54.
4. Friederich JA, Butterworth JF. Sodium nitroprusside: twenty years and counting. *Anesth Analg*. 1995 Jul;81(1):152–62.
5. Kanto J, Allonen H, Kleimola T, Mäntylä R. Pharmacokinetics of labetalol in healthy volunteers. *Int J Clin Pharmacol*. 1981 Jan;19(1):41–4.
6. Bünemann L, Jensen KA, Riisager S, Thomsen LJ. Cerebral blood flow and metabolism during hypotension induced with sodium nitroprusside and metoprolol. *Eur J Anaesthesiol*. 1991 May;8(3):197–201.
7. Cottrell JE, Gupta B, Rappaport H, Turndorf H, Ransohoff J, Flamm ES. Intracranial pressure during nitroglycerin-induced hypotension. *J Neurosurg*. 1980 Sep 1;53(3):309–11.
8. Cottrell JE, Patel K, Turndorf H, Ransohoff J. Intracranial pressure changes induced by sodium nitroprusside in patients with intracranial mass lesions. *J Neurosurg*. 1978;48(3):329–31.
9. Larsen R, Teichmann J, Hilfiker O, Busse C, Sonntag H. Nitroprusside-Hypotension: Cerebral Blood Flow and Cerebral Oxygen Consumption in Neurosurgical Patients. *Acta Anaesthesiol Scand*. 1982;26(4):327–30.
10. Griffiths DPG, Cummins BH, Greenbaum R, Griffith HB, Staddon GE, Wilkins DG, et al. CEREBRAL BLOOD FLOW AND METABOLISM DURING HYPOTENSION INDUCED WITH SODIUM NITROPRUSSIDE. *Br J Anaesth*. 1974 Sep;46(9):671–9.
11. Schroeder T, Schierbeck J, Howardy P, Knudsen L, Skafte-Holm P, Gefke K. Effect of labetalol on cerebral blood flow and middle cerebral arterial flow velocity in healthy volunteers. *Neurol Res*. 1991 Mar 1;13(1):10–2.
12. Dubois M, Caputy A, MacCosbe P, Lea D, Duma C. Cerebral blood flow measurements during blood pressure control with intravenous labetalol following craniotomy. *J Neurosurg Anesthesiol*. 1992 Jul 1;4(3):176–81.

13. Effect of Esmolol on Cerebral Blood Flow During Intracranial Hypertension and Hemorrhagic Hypovolemia | Anesthesiology | American Society of Anesthesiologists [Internet]. [cited 2023 Jun 26]. Available from: <https://pubs.asahq.org/anesthesiology/article/67/3/A424/45505/Effect-of-Esmolol-on-Cerebral-Blood-Flow-During>
14. Prielipp RC, Wall MH, Tobin JR, Groban L, Cannon MA, Fahey FH, et al. Dexmedetomidine-Induced Sedation in Volunteers Decreases Regional and Global Cerebral Blood Flow. *Anesth Analg*. 2002 Oct;95(4):1052.
15. Kaplan JA. Clinical considerations for the use of intravenous nicardipine in the treatment of postoperative hypertension. *Am Heart J*. 1990 Feb 1;119(2, Part 2):443–6.
16. Joshi S, Young WL, Duong H, Aagaard BA, Ostapkovich ND, Connolly ES, et al. Intracarotid nitroprusside does not augment cerebral blood flow in human subjects. *Anesthesiology*. 2002 Jan;96(1):60–6.
17. White RP, Deane C, Hindley C, Bloomfield PM, Cunningham VJ, Vallance P, et al. The effect of the nitric oxide donor glyceryl trinitrate on global and regional cerebral blood flow in man. *J Neurol Sci*. 2000 Sep 1;178(1):23–8.
18. Dihydralazine induces marked cerebral vasodilation in man - SCHROEDER - 1987 - European Journal of Clinical Investigation - Wiley Online Library [Internet]. [cited 2023 Jun 26]. Available from: <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1365-2362.1987.tb01238.x>
19. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. *J Neurosurg*. 1982 Dec;1;57(6):769–74.
20. Bellner J, Romner B, Reinstrup P, Kristiansson KA, Ryding E, Ryding E. Transcranial Doppler sonography pulsatility index (PI) reflects intracranial pressure (ICP). *Surg Neurol*. 2004 Jul;1;62(1):45–51.
21. Liu J, Zhu YS, Khan MA, Brunk E, Martin-Cook K, Weiner MF, et al. Global brain hypoperfusion and oxygenation in amnesic mild cognitive impairment. *Alzheimers Dement J Alzheimers Assoc*. 2014 Mar;10(2):162–70.
22. Smielewski P, Czosnyka M, Kirkpatrick P, McEroy H, Rutkowska H, Pickard JD. Assessment of Cerebral Autoregulation Using Carotid Artery Compression. *Stroke*. 1996 Dec;27(12):2197–203.
23. Blaivas M, Theodoro D, Sierzenski PR. Elevated intracranial pressure detected by bedside emergency ultrasonography of the optic nerve sheath. *Acad Emerg Med*. 2003;

24. Immink RV, Born BJ, Montfrans GA, Kim YS, Hollmann MW, Lieshout JJ. Cerebral hemodynamics during treatment with sodium nitroprusside versus labetalol in malignant hypertension. *Hypertension*. 2008;
25. Liu J, Zhu YS, Hill C, Armstrong K, Tarumi T, Hodics T, et al. Cerebral autoregulation of blood velocity and volumetric flow during steady-state changes in arterial pressure. *Hypertension*. 2013;
26. Gibson BE, Black S, Maass L, Cucchiara RF. Esmolol for the control of hypertension after neurologic surgery. *Clin Pharmacol Ther*. 1988 Dec;44(6):650–3.
27. Hartmann A, Buttinger C, Rommel T, Czernicki Z, Trtinjak F. Alteration of intracranial pressure, cerebral blood flow, autoregulation and carbondioxide-reactivity by hypotensive agents in baboons with intracranial hypertension. *Neurochirurgia (Stuttg)*. 1989 Mar;32(2):37–43.
28. Candia GJ, M.D. RCH, M.D. MHL, M.D. CNZ, M.D. CNN, M.D. Effect of Intravenous Sodium Nitroprusside on Cerebral Blood Flow and Intracranial Pressure. *Neurosurgery*. 1978 Aug;3(ue 1):50–3.
29. Michenfelder JD, Milde JH. The interaction of sodium nitroprusside, hypotension, and isoflurane in determining cerebral vasculature effects. *Anesthesiology*. 1988 Dec;69(6):870–5.
30. Thomas KN, Cotter JD, Galvin SD, Williams MJ, Willie CK, Ainslie PN. Initial orthostatic hypotension is unrelated to orthostatic tolerance in healthy young subjects. *J Appl Physiol*. 2009;107:506–17.
31. Brown MM, Wade JP, Marshall J. Fundamental importance of arterial oxygen content in the regulation of cerebral blood flow in man. *Brain J Neurol*. 1985 Mar;108 (Pt 1):81–93.
32. Guo H, Tierney N, Schaller F, Raven PB, Smith SA, Shi X. Cerebral autoregulation is preserved during orthostatic stress superimposed with systemic hypotension. *J Appl Physiol*. 2006;1;100(6):1785–92.
33. Simsic JM, Bradley SM, Mulvihill DM. Sodium nitroprusside infusion after bidirectional superior cavopulmonary connection: preserved cerebral blood flow velocity and systemic oxygenation. *J Thorac Cardiovasc Surg*. 2003 Jul;126(1):186–90.
34. Xu Z, Ren H, Huang Y, Zhang X, Luo A, Ye T. [The effects of sodium nitroprusside-induced hypotension at different levels on cerebral blood flow and metabolism: a clinical study]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*. 2000 Aug;22(4):360–3.

35. Olesen ND, Fischer M, Secher NH. Sodium nitroprusside dilates cerebral vessels and enhances internal carotid artery flow in young men. *J Physiol.* 2018 Sep 1;596(17):3967–76.
36. Schumann-Bard P, Touzani O, Young AR, Toutain J, Baron JC, Mackenzie ET, et al. Cerebrovascular Effects of Sodium Nitroprusside in the Anaesthetized Baboon: A Positron Emission Tomographic Study. *J Cereb Blood Flow Metab.* 2005 Apr 1;25(4):535–44.
37. Grubb RL, Raichle ME. Effects of hemorrhagic and pharmacologic hypotension on cerebral oxygen utilization and blood flow. *Anesthesiology.* 1982 Jan;56(1):3–8.
38. McDowall DG, Keaney NP, Turner JM, Lane JR, Okuda Y. The toxicity of sodium nitroprusside. *Br J Anaesth.* 1974 May;46(5):327–32.
39. Strebel S, Lam AM, Matta B, Aaslid MTS, R N, D.W. Dynamic and static cerebral autoregulation during isoflurane, desflurane, and propofol anesthesia. *Anesthesiology.* Vol. 83. 1995. p. 66–76.
40. Lucas SJE, Tzeng YC, Galvin SD, Thomas KN, Ogoh S, Ainslie PN. Influence of Changes in Blood Pressure on Cerebral Perfusion and Oxygenation. *Hypertension.* 2010 Mar;55(3):698–705.
41. Giller CA, Bowman G, Dyer H, Mootz L, Krippner W. Cerebral arterial diameters during changes in blood pressure and carbon dioxide during craniotomy. *Neurosurg.* 1993;32:737–41.
42. Role of nitric oxide in exercise-induced vasodilation of the forearm - PubMed [Internet]. [cited 2023 Aug 23]. Available from: <https://pubmed.ncbi.nlm.nih.gov/7994834/>
43. Vallance P, Collier J, Moncada S. Effects of endothelium-derived nitric oxide on peripheral arteriolar tone in man. *Lancet Lond Engl.* 1989 Oct 28;2(8670):997–1000.
44. Lavi S, Egbarya R, Lavi R, Jacob G. Role of Nitric Oxide in the Regulation of Cerebral Blood Flow in Humans. *Circulation.* 2003 Apr 15;107(14):1901–5.
45. Joshi S, Duong H, Mangla S, Wang M, Libow AD, Popilskis SJ, et al. In nonhuman primates intracarotid adenosine, but not sodium nitroprusside, increases cerebral blood flow. *Anesth Analg.* 2002 Feb;94(2):393–9, table of contents.

PROFORMA

TITLE:

Automated Pupillometry for Assessing Emergence from Anaesthesia in Supratentorial Craniotomy Patients: A Prospective Observational Study

AGE:

GENDER:

DIAGNOSIS:

PREOPERATIVE COMPLAINTS:

ASA GRADE:

DATE OF SURGERY:

BASELINE PARAMETERS:

HEART RATE:

BLOOD PRESSURE:

SPO2:

CHECKLIST

FACTORS	INCLUDE	EXCLUDE
Patient Consent	YES	NO
Nature of Surgery	ELECTIVE	EMERGENCY
Age	18-65	<18,>60
Long standing uncontrolled DM, hypertension on multiple drugs, liver disease, Ischemic heart disease, chronic renal disease, bronchial asthma or lung diseases	NO	YES
Pregnancy, postpartum, lactating females	NO	YES
Patients with preoperative cognitive dysfunction	NO	YES
History of preoperative anisocoria	NO	YES
History of cataract surgery, glaucoma, ocular trauma, tumours affecting optic and oculomotor pathway	NO	YES
Preoperative GCS less than 15	NO	YES
History of preoperative cognitive dysfunction	NO	YES
Hydrocephalus/Hematoma in Postoperative CT Scan	NO	YES

A. HAEMODYNAMIC PARAMETERS

	T0	T1	T2	T3
HEART RATE				
BLOOD PRESSURE				
SPO2				
PaCO2				
TEMPERATURE				

B. PUPILLOMETRY

	T0		T1		T2		T3	
	RT	LT	RT	LT	RT	LT	RT	LT
PUPILLARY SIZE								
NPI								
CV								
MCV								
LATENCY								
DV								

C. BIS

	T0	T1	T2	T3
BIS VALUE				
SEF				

D. ANAESTHESIA DETAILS

1. INDUCTION AGENT:
2. MAINTENANCE AGENT:
3. TOTAL OPIOID CONSUMPTION:
4. MUSCLE RELAXANT USED AND DOSE:
5. INTRAOPERATIVE BLOOD LOSS:
6. TIME FROM INDUCTION OF ANAESTHETICS TO TERMINATION OF ANAESTHETICS:
7. TIME FROM TERMINATION OF ANAESTHETICS TO INCREASE IN BIS VALUE OF 80:
8. TIME FROM TERMINATION OF ANAESTHETICS TO OPENING OF EYES TO VERBAL COMMAND:
9. TIME FROM TERMINATION OF ANAESTHETICS TO EXTUBATION:

- T0 – Baseline, prior to induction
- T1 – At point of termination of anaesthetic
- T2 – At the point BIS value increases to 80
- T3 – At point of opening of eyes to verbal command

NAME AND SIGNATURE OF THE INVESTIGATOR (with date):

PATIENT INFORMATION FORM

TITLE: Automated Pupillometry for Assessing Emergence from Anaesthesia in Supratentorial Craniotomy Patients: A Prospective Observational Study

Name of the Investigators:

Dr. Revikrishnan S (PI), Dr. Manikandan S (Guide and CO-PI), Dr Smita V (CO - PI), Dr Ajay Prasad Hrishu (CO-PI)

You are being requested to participate in the above titled study which is being conducted to evaluate the use of automated pupillometer as a tool for assessing awakening of patients from anaesthesia following supratentorial craniotomy.

Before you agree to participate in this study, it is important that you read and understand this patient information form which will provide you all the requisite information to clear your doubts and make a well-informed decision about your participation in the study. In addition, should you have any further questions, please feel free to ask us the same

We have planned to recruit people posted for elective supratentorial neurosurgical procedure at SCTIMST, Trivandrum.

What is Automated pupillometry?

Automated pupillometry is a way to measure the size and reaction of the pupils in your eyes using a special device. It's like a high-tech version of the flashlight test that doctors do, where they shine a light in your eyes and watch how your pupils change size. The device used for automated pupillometry is called a pupilometer, and it takes away the guesswork by giving precise and consistent measurements. This is really helpful because changes in pupil size and reaction can tell doctors a lot about what's going on in your brain,

What is BIS /BISPECTRAL INDEX?

BIS device consists of an adhesive electrode strip like a sticker placed on patient's forehead. The other end of the device will be connected to a monitor. This is used to monitor depth of sedation after giving the drug to the patient.

If you take part, what will you have to do?

On the day before surgery, your vital parameters viz. heart rate, blood pressure and oxygen saturation will be recorded. On the day of surgery, you will be taken inside the Operation Theatre. All routine non invasive monitors to check your heart rate, blood pressure and oxygen saturation level will be attached. BIS monitor will be attached to your forehead and baseline values will be recorded. Baseline pupillometric indices will be recorded prior to administering general anaesthesia to

you. On completion of the surgery, the anaesthetic drugs will be stopped and the BIS values and pupillometric values will be recorded again. We will continue to record BIS and pupillometric indices till you open your eyes and are able to follow simple commands.

What is the purpose of this study?

Assessing awakening from anaesthesia, particularly in neurosurgical patients, is crucial. Despite the lack of fool proof monitors or equipment, tools like Bis can be costly, require specialized interpretation skills, and come with their own drawbacks. If an automated pupillometer can demonstrate effectiveness comparable to BIS in evaluating awakening, it could offer a simpler and more affordable alternative.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way. In addition, if you experience any side effects, the study will be stopped and you will be given treatment for the side effects.

What will happen if you develop any study related injury?

We do not expect any injury to happen to you since the anaesthesia technique and monitoring tools would be same even if you were not part of the study. But if you do develop any side effects or problems due to the study, the side effects will be treated at no cost to you. We are unable to provide any monetary compensation, however.

Will you have to pay for the cost of using the test?

These are used as a part of anaesthesia procedure for surgery. No additional charges will be incurred for participating in the study.

Will your personal details be kept confidential?

The results of this study will be used for thesis submission as a part of academic research and will be submitted to a medical journal for publication, but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

When you read this information, your treating doctor will be available to discuss and answer any questions you may have. If you have any queries please contact:

Dr Revikrishnan S

Post-doctoral fellow, Division of Neuroanaesthesia, Department of Anaesthesiology

Sree Chitra Tirunal Institute for Medical Sciences and Technology Tel: +91

9895911697, Email: dr.revikrishnan@sctimst.ac.in

If you have any questions, concerns or complaints about the research please contact:

Dr. Srinivas G

Member Secretary, Institutional Ethics Committee,

Sree Chitra Tirunal Institute for Medical Sciences and Technology Tel: 0471-

2524689, Email: iec.mem.sec@sctimst.ac.in

പങ്കെടുക്കുന്നവർക്കുള്ള കാര്യവിവരണപത്രം

തലയുടെ മുകൾഭാഗത്തെ തലയോട്ടി വഴി (സുപ്രാടെന്റോറിയൽ ക്രേനിയോട്ടമി) നടത്തുന്ന ശസ്ത്രക്രിയയ്ക്ക് ശേഷം അബോധാവസ്ഥയിൽനിന്നും (അനസ്തീഷ്യ) ഉണരുന്നത് വിലയിരുത്തുന്നതിനുള്ള യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രി: ഭാവികാലപ്രാപ്യമായ ഒരു നിരീക്ഷണ പഠനം.

ഗവേഷകരുടെ പേര്:

ഡോ. രവീകൃഷ്ണൻ എസ് (പ്രധാനഗവേഷകൻ), ഡോ. മണികണ്ഠൻ എസ് (ഗൈഡും സഹപ്രധാനഗവേഷകനും), ഡോ. സ്മിത വി (സഹപ്രധാനഗവേഷക) ഡോ. അജയ് പ്രസാദ് ഋഷി (സഹപ്രധാനഗവേഷകൻ)

തലയോട്ടിയുടെ മുകൾഭാഗം വഴി നടത്തുന്ന ശസ്ത്രക്രിയയ്ക്ക് ശേഷം അബോധാവസ്ഥയിൽനിന്നും (അനസ്തീഷ്യ) ഉണരുന്നത് വിലയിരുത്തുന്നതിനുള്ള യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രിയുടെ പ്രയോജനക്ഷമത പഠിക്കുന്ന പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കളെ ഞങ്ങൾ ക്ഷണിക്കുന്നു.

പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കൾ സമ്മതിക്കുന്നതിന് മുമ്പ് താങ്കളുടെ സംശയങ്ങൾ ദുരീകരിക്കാനും കാര്യബോധത്തോടുള്ള തീരുമാനം എടുക്കാനും സഹായിക്കുന്ന ഈ കാര്യവിവരണപത്രം വായിക്കുകയും മനസ്സിലാക്കുകയും ചെയ്യേണ്ടത് പ്രധാനമാണ്. മാത്രമല്ല, താങ്കൾക്ക് കൂടുതലായി ചോദ്യങ്ങളെന്തെങ്കിലും ഉണ്ടെങ്കിൽ ദയവായി ഞങ്ങളോട് ചോദിക്കാനും മടിക്കരുത്.

തിരുവനന്തപുരം SCTIMSTയിൽ തീരുമാനിക്കപ്പെട്ട സുപ്രാടെന്റോറിയൽ ക്രേനിയോട്ടമി ശസ്ത്രക്രിയയ്ക്ക് വിധേയരാകുന്ന രോഗികളെ ഉൾപ്പെടുത്താൻ ഞങ്ങൾ ആസൂത്രണം ചെയ്യുന്നു.

യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രി എന്നാലെന്ത്?

ഒരു പ്രത്യേക ഉപകരണമുപയോഗിച്ച് താങ്കളുടെ കണ്ണിലെ കൃഷ്ണമണികളുടെ വലുപ്പവും പ്രതികരണങ്ങളും അളക്കുന്ന രീതിയാണ് യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രി. അത് താങ്കളുടെ കണ്ണുകളിൽ പ്രകാശം പതിപ്പിച്ച്, താങ്കളുടെ കണ്ണുകളുടെ വലുപ്പം നിരീക്ഷിക്കാൻ ഡോക്ടർമാർ ഉപയോഗിക്കുന്ന ഫ്ളാഷ്ലൈറ്റിനേക്കാൾ വളരെ ഉയർന്ന സാങ്കേതികതയുള്ള ഒരു പതിപ്പാണ്. യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രിക്കുപയോഗിക്കുന്ന ഉപകരണത്തിനെ പ്യൂപിലോമീറ്റർ എന്ന് വിളിക്കുന്നു, അയത് കൃത്യവും സ്ഥിരതയുള്ളതുമായ അളവുകൾ നൽകി ഊഹാപോഹത്തിന്റെ മാർഗ്ഗം ഒഴിവാക്കുന്നു. താങ്കളുടെ തലച്ചോറിൽ എന്ത് നടക്കുന്നു എന്ന് മനസ്സിലാക്കാൻ കൃഷ്ണമണിയുടെ വലുപ്പവും പ്രതികരണങ്ങളും ഡോക്ടറെ സഹായിക്കുമെന്നതിനാൽ ഇത് വളരെ ഉപയോഗപ്രദമാണ്.

എന്താണ് ബിഐഎസ്/ബിസ്പെക്റ്റൽ സൂചിക?

ബിഐഎസ് ഉപകരണത്തിൽ സ്റ്റിക്കറുപോലെ രോഗിയുടെ നെറ്റിയിൽ ഒട്ടിക്കുന്ന ഒരു ഇലക്ട്രോഡ് സ്ട്രിപ്പ് അടങ്ങിയിരിക്കുന്നു. ഉപകരണത്തിന്റെ മറ്റേഭാഗം ഒരു നിരീക്ഷണിയോട് (മോണിറ്റർ) ഘടിപ്പിച്ചിരിക്കുന്നു. രോഗിക്ക് മരുന്ന് നൽകിയതിനുശേഷം മയക്കലിന്റെ ആഴം നിരീക്ഷിക്കാൻ ഇതുപയോഗിക്കുന്നു.

താങ്കൾ പങ്കെടുക്കുകയാണെങ്കിൽ എന്തുചെയ്യണം?

ശസ്ത്രക്രിയയ്ക്കു മുൻപത്തെ ദിവസം, ഹൃദയമിടിപ്പ്, രക്തസമ്മർദ്ദം, പ്രാണവായുപുരിതാവസ്ഥ മുതലായ താങ്കളുടെ ജീവൽഘടകങ്ങൾ രേഖപ്പെടുത്തും. ശസ്ത്രക്രിയാദിവസം, താങ്കളെ ശസ്ത്രക്രിയാമുറിയിൽ പ്രവേശിപ്പിക്കും. താങ്കളുടെ ഹൃദയമിടിപ്പ്, രക്തസമ്മർദ്ദം, പ്രാണവായുപുരിതാവസ്ഥ മുതലായ ശരീരത്തിൽ കടക്കാതെ നിരീക്ഷിക്കുന്ന പതിവ് ഉപകരണങ്ങൾ താങ്കളിൽ ഘടിപ്പിക്കും. താങ്കളുടെ നെറ്റിയിൽ ബിഐഎസ് നിരീക്ഷണോപകരണം ഘടിപ്പിച്ച് അടിസ്ഥാന മൂല്യങ്ങൾ രേഖപ്പെടുത്തും. താങ്കൾക്ക് പൊതുവായ മയക്കം ഉണ്ടാക്കുന്ന മരുന്ന്

നൽകുന്നതിനുമുമ്പ് അടിസ്ഥാന പ്ലാപ്പിലോമെട്രിക് സൂചകങ്ങൾ രേഖപ്പെടുത്തും. ശസ്ത്രക്രിയപൂർത്തിയാകുമ്പോൾ, മയക്കൽ മരുന്ന് നിർത്തുകയും ബിഐഎസ് മൂല്യങ്ങളും പ്ലാപ്പിലോമെട്രിക് സൂചകങ്ങളും വീണ്ടും രേഖപ്പെടുത്തും. കണ്ണ് തുറക്കുകയും താങ്കൾക്ക് ലളിതമായ നിർദ്ദേശങ്ങൾ മനസ്സിലാക്കാൻ കഴിയുകയും ചെയ്യുന്നതുവരെ ബിഐഎസ്, പ്ലാപ്പിലോമെട്രിക് സൂചകങ്ങൾ രേഖപ്പെടുത്തുന്നത് തുടരും.

ഈ പഠനത്തിന്റെ ഉദ്ദേശമെന്ത്?

മയക്കത്തിൽ നിന്നും ഉണരുക എന്നത്, പ്രത്യേകിച്ചും ന്യൂറോശസ്ത്രക്രിയാ രോഗികളിൽ നിർണ്ണായകമാണ്. കുറ്റമറ്റ നിരീക്ഷണോപകരണങ്ങളുടെ അഭാവം ഉണ്ടെങ്കിലും, ബിഐഎസ് പോലുള്ള ഉപകരണങ്ങൾ ചെലവേറിയതും വ്യാഖ്യാനിക്കാൻ വൈദഗ്ദ്ധ്യം വേണ്ടുന്നതും പരിമിതികളോടുകൂടിയതുമാണ്. ഉണരുന്നത് വിലയിരുത്തുന്നതിൽ ഒരു യന്ത്രവൽകൃത പിപ്പിലോമീറ്ററിന് ബിഐഎസ് മുമായി താരതമ്യപ്പെടുത്താവുന്ന ഫലപ്രാപ്തി നൽകാൻ കഴിയുമെങ്കിൽ, ലളിതവും ചെലവ് താങ്ങാനാകുന്നതുമായ ഒരു ബദലാകാൻ കഴിയും.

പഠനമാരംഭിച്ചതിനുശേഷം താങ്കൾക്ക് പിൻമാറാനാകുമോ?

താങ്കളുടെ പങ്കാളിത്തം തികച്ചും സ്വമേധയായാണ്, ഏതുസമയത്തും താങ്കൾക്ക് പഠനത്തിൽനിന്നും പിൻമാറാൻ സ്വാതന്ത്ര്യമുണ്ട്. അങ്ങനെ ചെയ്യുന്നതുകൊണ്ട് താങ്കളുടെ ഈ ആശുപത്രിയിലെ ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല. താങ്കൾക്കെന്തെങ്കിലും പാർശ്വഫലങ്ങളുണ്ടായാൽ പഠനം നിർത്തുകയും പാർശ്വഫലങ്ങൾക്ക് ചികിത്സ നൽകുകയും ചെയ്യും.

പഠനവുമായി ബന്ധപ്പെട്ട് പരിക്കുണ്ടായാലെന്ത് സംഭവിക്കും?

താങ്കൾ പഠനത്തിൽ പങ്കെടുത്താലും ഇല്ലെങ്കിലും ഉപയോഗിക്കുന്ന മയക്കൽ സങ്കേതവും നിരീക്ഷണോപകരണങ്ങളും ഒന്നുതന്നെയാകയാൽ പഠനവുമായി ബന്ധപ്പെട്ട് എന്തെങ്കിലും പരിക്കുണ്ടാവുമെന്ന് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നില്ല. പക്ഷേ പഠനസംബന്ധമായി താങ്കൾക്കെന്തെങ്കിലും പാർശ്വഫലങ്ങളുണ്ടായാൽ താങ്കൾക്ക് ചെലവുണ്ടാകാതെ പാർശ്വഫലങ്ങൾ ചികിത്സിക്കും. എന്നിരുന്നാലും എന്തെങ്കിലും സാമ്പത്തിക നഷ്ടപരിഹാരം നൽകാൻ ഞങ്ങൾക്കാവില്ല.

പരിശോധനയ്ക്ക് താങ്കൾ പണം നൽകണോ?

മയക്കൽ നടപടികളുടെ ഭാഗമായി ഉപയോഗിക്കുന്നവയാണിവ. പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് അധികച്ചെലവ് ഉണ്ടാകില്ല.

താങ്കളുടെ വ്യക്തിവിവരങ്ങൾ രഹസ്യമായിരിക്കുമോ?

വൈജ്ഞാനിക ഗവേഷണത്തിന്റെ ഭാഗമായി ഈ പഠനഫലങ്ങൾ ഒരു ഗവേഷണ പ്രബന്ധത്തിനുപയോഗിക്കുകയും ഒരു വൈദ്യശാസ്ത്ര ജേർണലിൽ പ്രസിദ്ധീകരണത്തിന് നൽകുകയും ചെയ്യും, പക്ഷേ താങ്കളെ പേരുകൊണ്ട് ഒരു പ്രസിദ്ധീകരണത്തിലും ഫലങ്ങളുടെ പ്രദർശനത്തിലും തിരിച്ചറിയാനാവില്ല. എന്നിരുന്നാലും, താങ്കൾ പഠനത്തിൽ പങ്കെടുക്കാൻ തീരുമാനിക്കുകയാണെങ്കിൽ താങ്കളുടെ ചികിത്സാരേഖകൾ ഈ പഠനവുമായി ബന്ധപ്പെട്ടവർ, വിണ്ടുമുള്ള താങ്കളുടെ അനുവാദമില്ലാതെ അവലോകനം ചെയ്തേക്കാം.

താങ്കൾ ഈ വിവരങ്ങൾ വായിക്കുമ്പോൾ ചർച്ചചെയ്യാനും താങ്കൾക്ക് എന്തെങ്കിലും ചോദ്യമുണ്ടെങ്കിൽ ഉത്തരം നൽകാനുമായി താങ്കളെ ചികിത്സിക്കുന്ന ഡോക്ടർ ലഭ്യമായിരിക്കും.

താങ്കൾക്ക് കൂടുതലായി വിവരങ്ങൾ വേണമെങ്കിൽ ആരെ ബന്ധപ്പെടണം.

താങ്കൾക്ക് കൂടുതലായി വിവരങ്ങൾ വേണമെങ്കിൽ ദയവായി ബന്ധപ്പെടുക: ഡോ. രവീകൃഷ്ണൻ എസ്, പോസ്റ്റ് ഡോക്ടറൽ ഫെല്ലോ, ന്യൂറോഅനസ്തീഷ്യോളജി വിഭാഗം, അനസ്തീഷ്യോളജി ഡിപ്പാർട്ട്മെന്റ്, ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം

ഫോൺ. 91 9895911697 9 ഇമെയിൽ dr.revikrishnan@sctimst.ac.in

ഗവേഷണത്തെപ്പറ്റി പരാതികളോ, നിർദ്ദേശങ്ങളോ ഉണ്ടെങ്കിൽ താങ്കൾക്ക് ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റിയെ താഴെപ്പറയും വിലാസം ബന്ധപ്പെടാം.

ഡോ. ശ്രീനിവാസ് ജി, മെമ്പർ സെക്രട്ടറി, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി ഫോൺ 0471-2524689, ഇമെയിൽ iec.mem.sec@sctimst.ac.in

CONSENT FORM

Title: Automated Pupillometry for Assessing Emergence from Anaesthesia in Supratentorial Craniotomy Patients: A Prospective Observational Study

Participant's name:

Age (in years):

I _____, son/daughter of _____

Declare that (Please tick boxes)

- I have read the above information provided to me regarding the use of automated pupillometry for assessing emergence from anaesthesia in supratentorial craniotomy patients. []
- I have clarified any doubts that I had. []
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights []
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access []
- I understand that my identity will not be revealed in any information released to third parties or published []
- I voluntarily agree to take part in this study []
- I have been provided with the contact numbers of the principle investigator, in case I want to know more about the study and participants rights [].
- I received a copy of this signed consent form []

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Signature:

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

Name:

Signature:

Date:

സമ്മതപത്രം

തലയുടെ മുകൾഭാഗത്തെ തലയോട്ടി വഴി (സുപ്രാടെന്റോറിയൽ ക്രേനിയോട്ടമി) നടത്തുന്ന ശസ്ത്രക്രിയയ്ക്ക് ശേഷം അബോധാവസ്ഥയിൽനിന്നും (അനസ്തീഷ്യ) ഉണരുന്നത് വിലയിരുത്തുന്നതിനുള്ള യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രി: ഭാവികാലപ്രാപ്യമായ ഒരു നിരീക്ഷണ പഠനം.

പേര് _____ വയസ്സ് (വർഷത്തിൽ) _____ ആശുപത്രി നമ്പർ.....

ഞാൻ _____, മകൻ/മകൾ _____

(പ്രഖ്യാപിക്കുന്നതെന്തെന്നാൽ

(കോളങ്ങളിൽ അടയാളപ്പെടുത്തുക)

- തലയുടെ മുകൾഭാഗത്തെ തലയോട്ടി വഴി നടത്തുന്ന ശസ്ത്രക്രിയയ്ക്ക് ശേഷം അബോധാവസ്ഥയിൽനിന്നും (അനസ്തീഷ്യ) ഉണരുന്നത് വിലയിരുത്തുന്നതിനുള്ള യന്ത്രവൽകൃതമായ പ്യൂപ്പിലേമെട്രി: ഭാവികാലപ്രാപ്യമായ ഒരു നിരീക്ഷണ പഠനം സംബന്ധിച്ച് എനിക്ക് മുകളിൽ നൽകിയിട്ടുള്ള വിവരങ്ങൾ ഞാൻ വായിച്ചു. []
- എനിക്കുണ്ടായ സംശയങ്ങൾ പരിഹരിച്ചു. []
- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വയമേവയാണെന്നും, എന്റെപതിവ് ചികിത്സയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ എനിക്ക് ഏതുസമയത്തും പിൻമാറാൻ സ്വാതന്ത്ര്യമുണ്ടെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. []
- ഞാൻ പിൻമാറിയാലും പഠന സംഘത്തിനും, ഇൻസ്റ്റിറ്റ്യൂഷണൽ എത്തിക്സ് കമ്മിറ്റി അംഗങ്ങൾക്കും എന്റെ ആരോഗ്യരേഖകൾ പരിശോധിക്കാൻ എന്റെ സമ്മതം ആവശ്യമില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. അതിനു ഞാൻ സമ്മതിക്കുന്നു. []
- മൂന്നാം കക്ഷികൾക്ക് നൽകുമ്പോഴോ പ്രസിദ്ധീകരിക്കുമ്പോഴോ എന്റെ വ്യക്തിവിവരങ്ങൾ നൽകില്ലെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. []
- ഞാൻ പഠനത്തിൽ പങ്കെടുക്കുന്നതിന് സ്വയമേവ സമ്മതിക്കുന്നു. []
- പഠനത്തെപ്പറ്റിയും പങ്കെടുക്കുന്നവരുടെ അവകാശങ്ങളെപ്പറ്റിയും കൂടുതലറിയാൻ എനിക്ക് പ്രധാനഗവേഷകനെ ബന്ധപ്പെടാനുള്ള നമ്പർ നൽകിയിട്ടുണ്ട്. []
- ഈ പത്രികയുടെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് ലഭിച്ചു. []

പേര് _____

ഒപ്പ് _____

തീയതി _____

സാക്ഷിയുടെ പേര് _____

പങ്കെടുക്കുന്നയാളുമായുള്ള ബന്ധം _____

തീയതി

സമ്മതപത്രം വാങ്ങുന്നയാൾ

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവ്വഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണ പദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

ഗവേഷകനുവേണ്ടി

ഒപ്പ്

തീയതി

അനുവാദപത്രം

ശേഖരിക്കുന്ന

ആളുടെ പേര്

CV – Dr S Manikandan(Principal Investigator)

SETHURAMAN	MANIKANDAN	
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy): 09/03/1969		Sex: Male
Study Site Affiliation (e.g. Principal Investigator, Co-Investigator, Coordinator): Principal Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
DR S MANIKANDAN PROFESSOR, DIVISION OF NEUROANESTHESIA AND NEUROCRITICAL CARE DEPT OF ANESTHESIA SCTIMST, TRIVANDRUM		SCTIMST, TRIVANDRUM
Telephone (Office): 0471-2524575		Mobile Number: +91-9446334711
Telephone (Residence): +91-9446334711		Email: kanmanisethu@gmail.com
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
PDCC (NEUROANESTHESIA)	1999	SCTIMST, INDIA
MD (ANESTHESIA)	1998	MP SHAH MEDICAL COLLEGE, JAMNAGAR, INDIA
MBBS	1993	THANJAVUR MEDICAL COLLEGE, INDIA
Details of professional registration : Travancore-Cochin medical council Registration Number and Year of Registration: TCMC 67957		
Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
JULY 2012	PROFESSOR	SCTIMST, TRIVANDRUM
APRIL 2008	ADDITIONAL PROFESSOR	SCTIMST, TRIVANDRUM
APRIL 2005	ASSOCIATE PROFESSOR	SCTIMST, TRIVANDRUM
APRIL 2001	ASSISTANT PROFESSOR	SCTIMST, TRIVANDRUM
Brief summary of relevant research experience: 1. Has been guide for DM Neuroanesthesia students since 2011 2. Has over 80 publications 3. Authored 6 book chapters 4. Has both internal and external funded clinical projects and device development projects 5. Reviewer and editorial board member of Neuroanesthesia and Anesthesia journals		
Current project/s at hand: 1. Clinical projects: 7 2. Device development: 4		

V2.15042017

Signature: 	Date: 26 / 2 /2022 Place: TRIVANDRUM
--	---

V2.15042017

CV - Dr Revikrishnan S (Principal investigator)

Last Name: S	First Name: Revikrishnan	Middle Name
Date of Birth (dd/mm/yy) 10/06/88	Sex: Male	
Study Site Affiliation (e.g., Principal Investigator, Co-Investigator, Coordinator): Principal Investigator		
Professional Mailing Address (Include Institution name)	Study Site Address. (Include Institution name)	
Post-doctoral fellow, Division of Neuro Anaesthesia, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Science and Technology, Thiruvananthapuram, Pin: 696011	Division of Neuro Anaesthesia, Department of Anaesthesiology, Sree Chitra Tirunal Institute for Medical Science and Technology, Thiruvananthapuram, Pin: 696011	
Telephone (Office):	Mobile Number: 9895911697	
Telephone (Residence):	Email: revikrishnan@gmail.com	
Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
DM	2023	SCTIMST, Trivandrum
Diplomate of European Society of Anaesthesia and Intensive Care	2018	European Society of Anaesthesia, Brussels
MD	2017	Govt Medical College, Trivandrum
MBBS	2012	Govt Medical College, Trivandrum
Details of professional registration: (MCI/State Registration/Bar Council/DCI/etc including Registration Number and Year of Registration) TCMC NO: 46529, year: 2012		
Current and previous positions (most recent position first)		
Month and Year	Title	Institution/Company, Country
From January 2021 till	Senior resident, Division of Neuro anaesthesia	SCTIMST, INDIA
July 2019 to December 2020	Senior Resident, Dept of Anaesthesiology	ESIC Hospital, Udyogamandal, Ernakulam
October 2018 – June 2019	Assistant Professor, Dept of Anaesthesiology & Critical Care	Annapoorna Medical College & Hospital Salem
August 2017 – September 2018	Senior Resident, Dept of Anaesthesiology & Critical Care	Govt Medical College, Trivandrum
Brief summary of relevant research experience:		
- Sreekumar R, Hrish AP, Sethuraman M. Role of multimodal monitoring in the management of patients undergoing complex intracranial bypass procedures - A case series and literature review. Indian J Anaesth. 2023 Aug;67(8):743-746. doi: 10.4103/ija.ija_286_23. Epub 2023 Aug 15. PMID: 37693016; PMCID: PMC10488588. - Praveen R, Sethuraman M, Vimala S, Prathapadas U, Hrish AP, Nair P, Surendran S, Ahuja A, Sreekumar R, Vishnu B, Gowtham M. A prospective-randomized placebo-controlled trial comparing the effects of nebulized dexmedetomidine v/s dexmedetomidine-lignocaine mixture on intraoperative hemodynamics and surgical field quality in patients undergoing endoscopic transnasal transsphenoidal pituitary tumor surgery. Surg Neurol Int. 2023 Dec 15;14:431. doi: 10.25259/SNI_858_2023. PMID: 38213443; PMCID: PMC10783663.		
Signature: 		Date: 23.04.2023 Place: Trivandrum