**The use of BIS in comparison to limb-isolation technique to predict awareness in ECT: A pilot study**

## Project Team Roles and Responsibilities

Title: Dr Laura Mackenzie

Position: Critical Care Senior Resident Medical Officer, John Hunter Hospital

Qualifications: Bachelor of Medicine

Experience:

* 3 months anaesthetic experience, including in ECT
* Involvement in assisting in research since 2016

Team role: Coordinating Principal Investigator

Responsibilities: Project design, participant recruitment and obtaining consent, data collection, data analysis, report writing, literature review

Title: Dr Allysan Armstrong-Brown

Position: Director of Anaesthetics, Calvary Mater Hospital Newcastle

Qualifications: Bachelor of Medicine

Experience:

* 30 years of experience in anaesthesia, with ECT experience throughout that time
* Subspecialty in neuroanaesthesia

Team role: Principal Investigator

Responsibilities: Project design, data analysis, publication writing, literature review

Title: Dr Hamish Meares

Position: Anaesthetist, Calvary Mater Hospital Newcastle

Qualifications: Bachelor of Medicine, Masters in Biomedical Engineering

Research experience:

* 15 years anaesthetic experience doing ECT
* Involvement in assisting in various clinical trials since 1991
* Experience in statistics for clinical trials

Team role: Investigator

Responsibilities: Project design, data analysis, publication writing,  literature review

There are no financial or non-financial interests to disclose.

## Resources

This project will be a small pilot study conducted at Calvary Mater Newcastle. Each participant will require bispectral index (BIS) monitoring during electroconvulsive therapy (ECT). We have permission from the Director of Anaesthetics at Calvary Mater Newcastle to run the pilot study and use BIS equipment from the department. No further equipment is required. No additional funding/support is being sought or secured.

## Background

Introduction

Electroconvulsive therapy (ECT) is a well recognised treatment for severe psychiatric illness, including major depressive disorder, schizophrenia, bipolar disorder and catatonia which is delivered under general anaesthetic. Awareness is a rare complication of general anaesthetic whereby the patient experiences consciousness to events during the operation.(1) The Calvary Mater Hospital routinely provides anaesthetic for ECT. In order to monitor for awareness during ECT, the limb isolation technique is utilised. This involves muscle relaxant being administered after a limb tourniquet is tightened, therefore the isolated limb is not paralysed. Prior to treatment, the patient is asked to move their isolated limb and if movement occurs, they are deemed to require deeper anaesthetic prior to treatment in order to reduce the risk of awareness. The bispectral index (BIS) is a depth of anaesthesia monitor, which displays a real-time electroencephalopgraphy (EEG) trace and generates a dimensionless number from 0-100 from frontotemporal electrodes. The probability of postoperative recall is low when BIS is kept <60 intra-operatively. (2) Our objective in this pilot study is to assess the utility of BIS compared to limb-isolation technique to determine when a patient is appropriately anaesthetised to receive ECT and reduce the risk of awareness.

**Literature review**

Literature search

Databases: Cochrane, EMBASE, PUBMED

Search terms:

* Limb isolation technique
* Isolated limb technique
* Isolated forearm technique
* BIS or bispectral index and ECT or electroconvulsive therapy
* Entropy and ECT or electroconvulsive therapy
* ECT or electroconvulsive therapy and awareness

Search history:

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| Search date | Search engine | Search terms | Results |
| 31/5/21 | Cochrane | Limb isolation technique | 3 |
| 31/5/21 | Cochrane | Isolated limb technique | 3 |
| 31/5/21 | Cochrane | BIS or bispectral index ‘AND’ ECT or electro convulsive therapy | 19 |
| 31/5/21 | Cochrane | Entropy ‘AND’ ECT or electroconvulsive therapy (title abstract keyword) | 0 |
| 26/9/21 | Cochrane | Isolated forearm technique (title abstract keyword) | 63 |
| 31/5/21 | PubMed | Limb isolation technique (title/abstract) | 5 |
| 31/5/21 | PubMed | Isolated limb technique (title/abstract) | 0 |
| 31/5/21 | PubMed | BIS or bispectral index AND ECT or electroconvulsive therapy (title/abstract) | 42 |
| 31/5/21 | PubMed | Entropy AND ECT or electroconvulsive therapy (title/abstract) | 13 |
| 26/9/21 | PubMed | Isolated forearm technique (title/abstract) | 79 |
| 26/9/21 | EMBASE via Ovid | Limb isolation technique | 0 |
| 31/5/21 | EMBASE via Ovid | Isolated limb technique | 0 |
| 31/5/21 | EMBASE via Ovid | ECT or electroconvulsive therapy AND BIS or bispectral index | 22 |
| 31/5/21 | EMBASE via Ovid | ECT or electroconvulsive therapy AND entropy | 4 |
| 26/9/21 | EMBASE via Ovid | Isolated forearm technique | 47 |
| 4/10/21 | EMBASE via Ovid | (ECT or electroconvulsive therapy) AND awareness (title) | 10 |
| 4/10/21 | Cochrane | (ECT or electroconvulsive therapy) AND awareness (title/abstract) | 22 |
| 4/10/21 | PubMed | (ECT or electroconvulsive therapy) AND awareness (title/abstract) | 66 |
|  |  |  | 398 |

****PRISMA diagram:

Articles retrieved:

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**Null hypothesis**

A BIS reading of <60 correlates with no movement of isolated limb when administering ECT under general anaesthetic, therefore BIS monitoring does not alter decision to treat in comparison to limb isolation technique.

**Expected outcomes**

We expect that BIS reading will not consistently be <60 with no movement of the isolated limb when administering ECT under general anaesthetic.

## Project design

**Project setting**

This project will be conducted at Calvary Mater Hospital Newcastle.

**Project method**

Observational research

**Outcome measures**

BIS reading and isolated limb movement during ECT treatment

**Method for data collection**

1. An individual will be identified as a potential participant by the mental health team
2. The mental health team will inform the potential participant that a research project is underway and that they may be spoken to about whether the project may be suited to them and to discuss whether they are interested in participating. If the potential participant does not want to be approached, they will not be approached by the research team
3. If the potential participant is willing to discuss the research project, a member from the project team will discuss the research project with them.
4. If the potential participant would like to partake, their written consent will be obtained. If the potential participant does not provide consent, they will not be included in the study.
5. The participant will be introduced to the observer prior to their treatment
6. In the operating theatre, a BIS monitor will be applied to the participant in addition to routine monitoring for ECT
7. The treating anaesthetist will be blinded to BIS output
8. Otherwise, the participant will receive standard care according to routine clinical practice
9. The BIS output will be recorded at the time the patient is asked to move the isolated limb (multiple readings will be recorded if required due to positive limb movement and thus further administration of anaesthesia)
10. The observer will note whether there was response to the request to move the isolated limb and whether further anaesthesia was required prior to stimulus
11. Data collection and participant involvement in the study will be completed at the end of their ECT treatment
12. Consent will be confirmed verbally if an individual is going to be observed during another ECT treatment

**Study numbers**

During our pilot study, we will aim to observe 50 ECT treatments.

Literature suggests that the incidence of a positive test when using the isolated forearm technique is 34%(3). Clinicians who work at Calvary Mater Hospital providing anaesthetic for ECT estimate at least 10% of patients having ECT will move their isolated limb to command.

Given this is a pilot study, we believe a formal sample-size calculation is not appropriate. However based on literature and experience, we expect observing 50 ECT treatments will be adequate for out pilot study and will allow us to test our study protocol and assess feasibility for future research projects.

**Participants**

* Individuals having voluntary ECT at Calvary Mater Hospital Newcastle
* Inclusion criteria
	+ Individuals having ECT for major depressive disorder
* Exclusion criteria
	+ Indication for ECT other than major depressive disorder, including schizophrenia, schizoaffective disorder, bipolar disorder, catatonia, active psychosis
	+ Treatment with anti-epileptic medication

**Participant recruitment strategies and timeframes**

* Sampling strategy: convenience sampling
* Individuals who meet inclusion and exclusion criteria will be identified in discussion with the ECT mental health team at Calvary Mater Hospital Newcastle
* Potential participants will be informed that a research study is being completed and that they may be asked to participate by their mental health team. If an individual expresses to their mental health team that they do not want to be approached to discuss the research project, we will not approach them
* We will confirm with the mental health team that potential participants are voluntarily having ECT and have capacity to discuss and consent to participate in a research project prior to approaching them
* The CPI or member of the research team will approach a potential participant in person to discuss the research study
* Participants will be approached at the hospital prior to their ECT treatment. If they would like to participate and consent, they will be observed the same day. Potential participants will have the option to consider participation over days to weeks, and can be followed up at their next ECT appointment
* We will practice with cultural safety, including the following:
	+ - We will utilise interpreters to discuss the research project and gain consent from individuals from a linguistically diverse background
		- We will offer support from Aboriginal Liaison Officer to individuals who identify as being Aboriginal or Torres Strait Islander

**How will the research project accommodate people with a mental illness?**

* All participants in our observational study will have a mental illness, as this is the indication for them to be having ECT. We will treat all individuals with respect and dignity.
* We acknowledge that individuals with a mental illness may be at increased susceptibility to some forms of discomfort or distress. However, the additional BIS monitoring in our study involves no change to the patients standard ECT treatment and therefore we do not foresee that any participant will experience harm, discomfort or distress.
* If an individual becomes distressed when discussing the research project, we will not continue to discuss or try to consent the individual to participate. We will ensure the individual is supported, and there will be mental health professionals available if required when discussing the research project with potential participants.
* We acknowledge that an individuals first ECT treatment can be particularly stressful and confronting. Therefore, we will not approach individuals having their first ECT treatment to discuss the research project.
* The participants' degree of mental illness will have been assessed by their mental health provider prior to commencing ECT treatment and prior to their involvement in our study.
* We will continually observe for any evidence of discomfort or distress. We will also be open to feedback from the hospital staff and mental health team, in order to identify any issues and manage appropriately.

**Ethical considerations relevant to recruitment of people with a mental illness who participating in our research**

* The potential for coercion will be limited by emphasising an individual's right to choose to participate or not participate in the study, and avoid over emphasising the potential benefits of the study
* We acknowledge the potential impact of existing relationships on recruitment, including that our research team are doctors and the participants are individuals who are receiving mental health care. When recruiting, our role as researchers will be explained and our role as medical professionals will not be emphasised to influence an individuals decision to participate
* We will emphasise that the potential participant’s ECT treatment will not differ depending on whether they choose to participate or not
* An individual’s privacy will be respected. Confidentiality will be maintained at all times.
* Recruiters will be familiar with the guidance provided by the National Statement
* No money or incentives will be utilised in this study, therefore they will not impact upon recruitment
* We acknowledge that individuals with mental illness may be at increased risk to harm or discomfort. Because of this, we will undertake the consent process in an low pressure environment with plenty of time to ask questions
* The potential participant will be approached prior to entry to the treatment room to reduce the risk of coercion

**Consideration of bias**

1. Selection bias

Selection bias may impact our study, as we are using convenience sampling strategy and are not randomly selecting participants. We will be selecting participants who are having ECT and who are willing and consent to participate. By doing this, our study is exposed to volunteer bias, as our sample may not represent all participant characteristics, such as age or sex. However, this is the only feasible sampling strategy for our pilot study.

Using the same population to source participants and the prospective study design help to eliminate further selection bias.

2. Observer bias

The observer recording data during the study will not be blinded. However, given the data we are recording is objective, we predict that the influence of observer bias on our results will be minimal.

3. Interviewer bias

Given the study design, there is no potential for interview bias.

4. Recall bias

Given the prospective nature of our study, there is no potential for recall bias.

5. Measurement error

The objective measures being recorded during the study reduces the risk of measurement error. Results will be recorded in real time to further reduce the risk of error.

**Risks and burdens associated with the research project**

We acknowledge that individuals with a mental illness may be at increased susceptibility to some forms of discomfort or distress. However, a BIS monitor is a very low risk device that will not cause harm, discomfort or inconvenience. There will be no other changes to their ECT treatment. Any information collated about the individual will be coded and stored safely to ensure no personal information is leaked or disclosed, therefore minimising the risk to reputation.

There will be a small burden placed on the anaesthetist providing ECT treatment to the participants, as they will be required to place BIS monitoring on each patient. This takes approximately 30 seconds. BIS monitoring is not routine in ECT. However, BIS monitoring is a common device used in anaesthetics that is easily attached and causes no harm to individuals.

We do not foresee any risks or burdens to researchers or other third parties.

No significant personal relationships between participant and observer will develop given the short amount of time during which the participant and observer interact, and that majority of observation is undertaken while the participant is having ECT.

There are no concerns to the research project regarding political or institutional sensitivities.

**Benefit of research project**

Our objective in this pilot study is to assess the utility of BIS compared to limb-isolation technique to determine when a patient is appropriately anaesthetised to receive ECT and reduce the risk of awareness. This is further described in the 'Introduction' of our project protocol.

If significant utility of BIS monitoring is suggested in our pilot study, it will:

- Benefit individuals having ECT, as BIS may reduce the risk of awareness

- Benefit the anaesthetist, as it may provide guidance on appropriate and safe management of patients having ECT

- Promote further research

There are limited prior research studies investigating the use of BIS in comparison to limb-isolation technique to monitor for awareness. Our literature search has identified only four prior small cohort and observational studies (4-7). The use of BIS in comparison to limb-isolation technique to monitor for awareness has not been studied in the population of individuals having ECT. Rates of awareness in individuals having ECT is not well documented. Our literature search has only identified three case reports (8-10). Therefore, there is uncertainty around this topic within the anaesthetic community and there is potential for improvement in clinical practice from our research project.

These benefits illustrate why this research project should be undertaken. There are no significant risks or burdens associated with the research that need to be justified.

**Approach to provision of information to participants and/or consent**

Participants will be provided with written information and written consent will be sought prior to their involvement in the research study. If the participant consents to treatment, they will be observed the same day. Consent will be obtained by a research team member.

We acknowledge the right of a prospective participate to decline partaking in research and will not coerce anyone into participating.

An interpreter will be utilised for anyone whose primary language is other than English.

Participants in the study will be individuals who are voluntarily having ECT as part of their mental health management plan. This means they have been deemed to have capacity to provide consent to ECT by their mental health provider. Therefore, these participants should also have capacity to consent to participate in our study. This will be confirmed via discussion with the mental health team.

We acknowledge that an individuals mental health and ability to provide consent can vary over time. Therefore, when consenting each participant to partake in the study, we will evaluate their ability to provide informed consent.

According to the Australian Commission on Safety and Quality in Healthcare, to be able to provide informed consent, an individual must be able to:

- Understand the facts involved
- Understand the treatment choices
- Understand how the consequences of treatment affect them
- Retain the information and recall the details
- Weigh up the consequences of those choices, including the choice to refuse treatment
- Communicate their decision and understanding of its implications.

If an individual is not able to do the above, they will not be deemed capable to provide consent to participate in the research.

After providing written consent and being observed during an ECT treatment, consent will be reconfirmed verbally prior to a participant being observed at a subsequent ECT session.

We will respect any religious or cultural beliefs that impact an individual's decision to partake in research.

Potential participants will be given the opportunity to take time to consider whether they would like to participate in our research project. This will give them time to talk to family or friends if desired. They will be followed up at their next ECT session to further discuss whether they would like to participate.

The research team will keep record of participants that have refused to participate so they do not get approached at subsequent appointments.

**Research activities (participant commitment, project duration, participant follow-up)**

If an individual consents to participate in the study, they will be monitored with BIS monitoring during their anaesthetic for provision of ECT. The BIS output will be recorded during the provision of their anaesthetic by an observer. Details of the time and whether there was limb movement will also be recorded during the treatment. There will be no alterations to their standard ECT treatment. BIS monitoring will not impact on their ECT treatment or the provision of anaesthetic. Also, the study will not change the timeframe of their ECT treatment.

It will take approximately 20minutes (the duration of a standard ECT treatment) to observe and collect data for each participant.

We estimate that it will take 3 months to recruit participants for the study.

No participant follow-up will be required for this observational study.

**Data collection/gathering (including impact of and response to participant withdrawal)**

The information that will be gathered about each patient include:

* De-identified medical record number
* Indication for ECT
* American Society of Anaesthetists classification of physical health
* Age
* Sex
* BIS output and EEG trace
* Isolated limb movement

Information about each patient will be collated from:

* The participant
* Health records, once consent is obtained
* Observation during the study

Participant identifiable data (eg name, date of birth, address) will be replaced with their hospital medical record number in our records. No participant identifiable data will be stored.

If participants withdraw from the study prior to publication, we will delete all data and respect their decision. If we are still in the process of participant recruitment, we will extend recruitment to ensure we have adequate participant numbers.

**Data storage**

The data collected will be stored on a password protected device. We will be utilising the Hunter New England Health District REDCAP service. No hard copy data will be stored. Only the research team will have access to the data. We believe this will reduce the potential harm associated with collecting and utilising participants data for our research.

The data will stored safely for 15 years after completion of the study and then will be destroyed. Data will be stored on REDCAP.

There will be no secondary use of the collected information.

**Ethical considerations of the collection and use of data**

* We will be collecting personal and health information about participants. This will be gathered by the research team via participant interview, from health records, from health care teams and via direct observation. We will be recording personal and sensitive health information about participants in a re-identifiable coded manner (using the hospital medical record number).
* Utilising health records for research purposes is an alternative and secondary use for that information. We acknowledge that an individual's health record is private, and it is a privilege for a participant to give us consent to access this information. We will ensure we are explicit in our consent process so that participants are aware that we will be accessing their health record during the study.
* We understand there is a risk to a participants privacy and reputation by recording information, if it was to be misused. However, we will be mitigating this risk by recording data in a coded manner. No personal identifiers will be recorded during the research project.
* There are no conditions imposed by a third party. The information gathered in this project will not be converted into health information.
* We will adhere to the ethical principals of Section 1 of the National Statement, by acting with beneficence, integrity and respect.

**Secondary or incidental findings**

The BIS is a single piece of monitoring and the utility is unknown in ECT anaesthesia. Therefore, we do not foresee any secondary of incidental findings arising from our research project.

**Data analysis**

* Our review of collected data will identify whether there is correlation between BIS reading <60 and no limb movement prior to ECT treatment for each participant
* As this is a pilot study, we will not be analysing our data using statistical methods

**Data linkage**

* No data linkage is planned

## Results, outcomes and future plans

**Plans for return of results or findings of research to participants**

Participants will be given an option on the consent form to request a summary of the results when the project is completed. If they tick ‘yes’, they will be emailed a lay-summary fo the results when the project is completed.

If an individual who initially declined to receive a summary of results changes their mind, a copy of the summary will be provided to them.

The summary will be distributed via email. If a participant does not have an email address, a postage address will be recorded to facilitate distribution. The comprehension level of the document will reflect the Participant Information Statement.

Participant confidentiality will be maintained via the following methods:

* An individual email/letter will be distributed. Group emails will not be distributed.
* No identifiable information will be released on the summary
* The participant will not be identified as a participant in correspondence

**Plans for dissemination and publication of project outcomes**

* We plan to disseminate project outcomes to the anaesthetic staff and ECT staff working at Calvary Mater Hospital Newcastle
* We also plan to publish this study in a peer-reviewed journal
* Furthermore, we would like to present the project outcomes at the Royal Australian and New Zealand College of Psychiatrists Section of ECT and Neurostimulation Conference
* We may present the project outcomes at further Australian anaesthetic or psychiatry conferences/meetings if relevant

**Other potential uses of the data at the end of the project**

* Currently we do not foresee any other uses of the collated data at the end of the project

**Project closure processes**

* The commencement and closure of the project will be clearly communicated to the project site

**Plans for sharing and/or future use of data and/or follow-up research**

* We do not forsee any future use of the data collected during this project.
* If this pilot study suggests utility of BIS monitoring, this may inform the design of a future project. The raw data from this project will not be used in the future project.

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