VERSION NO:1
VERSION DATE: 15th July 2025

UNIVERSITY OF MALAYA MEDICAL CENTRE

RESEARCH PROTOCOL

1. Particulars of Researcher

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2. List of Co-researchers (Include all who have participated in the drafting of this proposal)

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3. **Research Proposal**

TITLE OF RESEARCH PROPOSAL

A Novel Transcutaneous Electrical Nerve Stimulation (TENS) Device in Patients Post Gynaecology Surgeries: A Triple-Blind, Placebo-Controlled Counterbalanced Crossover Trial

KEY WORDS

Novel transcutaneous electrical nerve stimulation (TENS) device
Gynaecology Surgeries

BACKGROUND/ JUSTIFICATION

Recent advances in pain management suggest that the optimal treatment requires interfering with multiple targets on pain pathways, known as multimodal analgesia. This approach utilizes a combination of interventions, each working on a different mechanism of pain to reach maximal pain relief using the lowest effective doses of medications. In addition to medication therapy, there are adjunctive physical and behavioral techniques such as massage therapy, physical therapy, and transcutaneous electrical nerve stimulation (TENS) therapy. According to a study by Baldini G et al, using both pharmacologic and non-pharmacologic interventions can improve pain control, enhance recovery, and increase patient satisfaction. Based on another study by Johnson MI, TENS can be used as an effective adjunct for managing postsurgical pain and to minimize the need for opioid and non-opioid analgesics as part of a multimodal approach to pain.
While the basic premise of TENS has remained relatively consistent, advancements in the device technology have led to more sophisticated devices that can target different nerve pathways, offering potential for more effective pain relief. The evidence for the use of these novel TENS devices in controlling pain is still evolving. This study aims to evaluate the analgesic efficacy and patient acceptability of a novel TENS device in the post-operative period.

OBJECTIVES/OUTCOMES

To evaluate the impact of a novel TENS device on short term pain score during movement at day 1 post gynaecology surgery through a counterbalanced crossover trial : immediately, 1 ,2 and 4 hours after novel TENS application using a 0-10 Numerical Rating Scale (11 point NRS).

Primary outcome:
Pain score on movement immediately, 1, 2 and 4 hours (a total of 4 measures) after application of active-TENS vs sham-TENS sessions using 0-10 numerical rating scale (11 points NRS): higher score indicates greater pain.

Secondary outcomes:

1. Repeated measures of the variance analysis for the serial pain scores across active-TENS vs sham-TENS sessions
2. Comparison of pain score on movement- immediately, 1, 2 and 4 hours after application of intervention or sham control sessions of 15 minutes after the first session only (across randomised arms).
3. Repeated measures of the variance analysis of the serial pain scores on movement (across randomised arms).
4. Identical analyses for similarly recorded blood pressure and pulse- immediately, 1, 2 and 4 hours after active-TENS vs sham-TENS sessions
5. Satisfaction score with the intervention immediately after the sessions, using 11 points NRS (higher score greater satisfaction)
6. Opioid consumption after application of active-TENS vs sham-TENS device

METHODOLOGY

Study design
This study will employ a randomized, triple-blind, placebo-controlled counterbalanced crossover trial design with 4 hours wash out period. This design allows each participant to serve as their own control, enhancing the reliability of the results as there is no control inter-subject variability at the same time minimising recruitment and outcome ascertainment bias.

Duration
18 months

Setting
Tertiary University Hospital, Gynaecology ward

Participants
The study population will consist of eligible and consented adult women at Day 1 post gynaecological surgery.

Inclusion criteria :
- Age ≥ 18 years old
- Patients undergoing elective or emergency gynaecology surgery (eg: myomectomy, hysterectomy, ovarian/ tubal surgeries) via transverse suprapubic incision under general anaesthesia
- Able to communicate in English or Malay
- Able to provide informed consent

Exclusion criteria :
- Contraindications to TENS (pacemaker, skin lesions)
- Chronic pain on regular opioids

Sample size
- Using Power and Sample Size program, assuming a one-point difference in the 11 points-NRS pain score at each of the four assessment points of immediately after, 1, 2, and 4 hours to be clinically relevant, pain score standard deviation is uniformly at 2.5 at all assessment points, alpha 0.0125(Bonferroni correction for 4 primary outcomes) and power of 95%.
- We will need to study 110 pairs of results. Hence we intend to recruit 110 participants, each participant providing a pair of pain scores at each assessment point following crossover.
- The Bonferroni correction to the p value and the 95% power is statistically conservative, intended to reduce both Type 1 and 2 errors.

Randomization
-Randomization will be performed using computerized sequence generator.
-The sequence will be generated in random blocks of 4 or 8 (1:1 ratio) via https://www.sealedenvelope.com/simple-randomiser/v1/lists by a co-investigator not involved in the trial recruitment.
-Participants will be assigned to one of two trial arms by opening a numbered, sealed, opaque envelope, with the lowest numbered envelope available assigned to the latest recruit.
ARM 1 : TENS followed by SHAM-CONTROL after a 4 hour gap
Or
ARM 2 : SHAM-CONTROL followed by TENS after a 4 hour gap

Blinding
- Participants
- Providers administering the TENS or sham-controlled treatment first
- Assessors who will evaluate outcomes and collect the feedbacks

To minimize bias and control for placebo effect, a triple-blind design will be employed: 3rd person who is not the provider nor the assessor will control the frequency to be delivered.

TENS device

The Remedius ExStim Pro will be used to deliver external non-invasive stimulation through the Integrated Duo Stimulating Wand. The intervention will be administered by provider after undergoing training on device application by the investigator.
A sham-shock with frequency of 100Hz with amplitude 5mA will be delivered for 30s at the subumbilical region at the start of each session to further enhance the sham and blinding process.
The TENS intervention will be delivered as follows:

TENS Parameters

1. **Frequency**: 100 Hz
2. **Pulse width**: Medium
3. **Amplitude**: 5 mA
4. **Duration**: Two TENS devices will be used simultaneously, each targeting one site at a time. Each site will be treated for 5 minutes, with two sites treated simultaneously. This will be repeated for 3 rounds, ensuring all 6 application sites are covered, requiring a total duration of 15 minutes per session.

Timing of Intervention:
The TENS intervention will be initiated on Day 1 (morning after) post gynaecology surgeries.

Intervention protocol

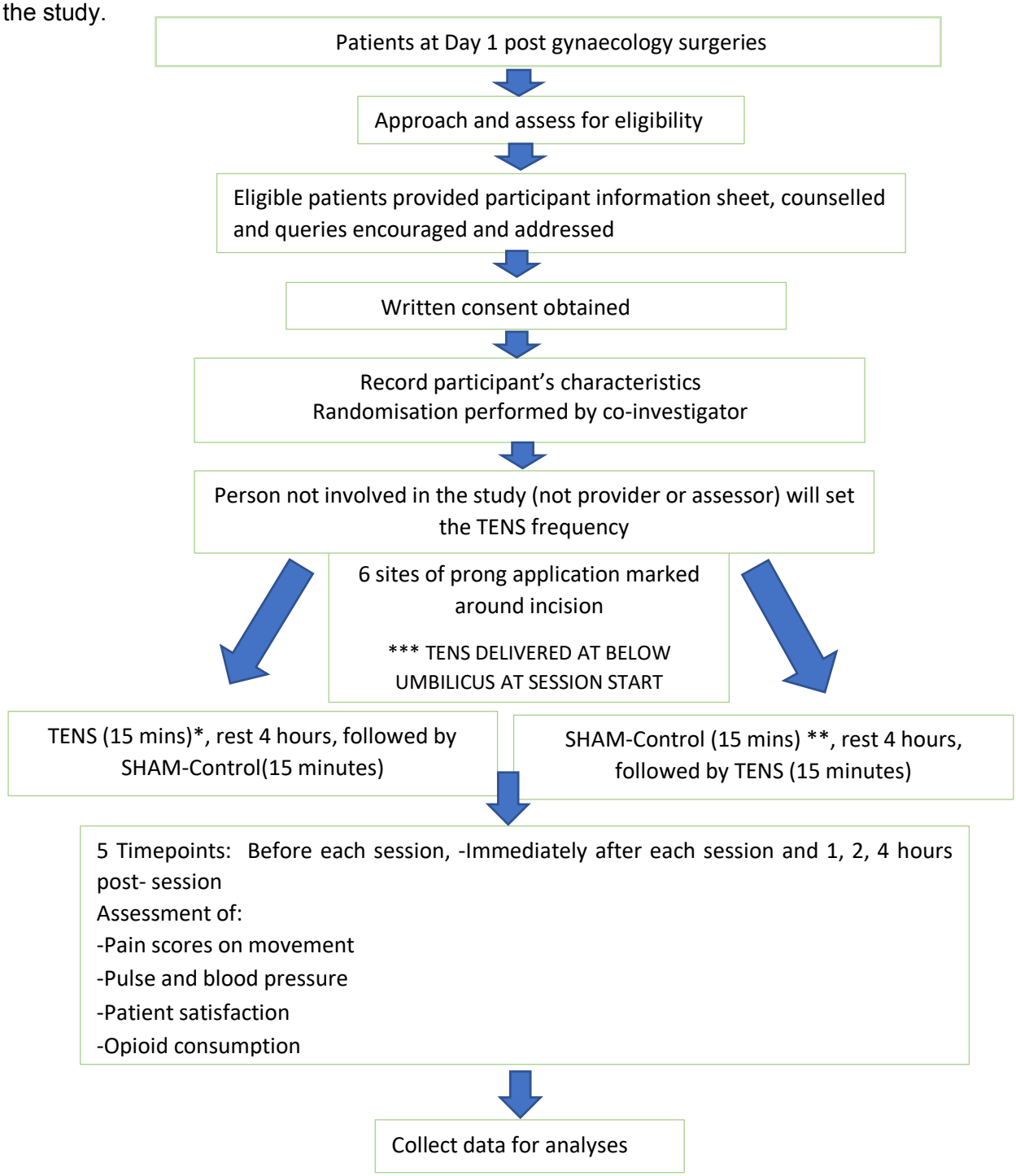
TENS First: Participants will receive TENS therapy at a frequency of 100 Hz and 5 mA intensity (set at medium pulse width). The TENS device will be applied at 6 fixed points for 5 minutes each, 1-2 cm lateral to wound edge and 1-2 cm above along, covering the transverse suprapubic incision. After 4 hours wash out, the same TENS device will be used in exactly the same manner with output at sham setting 0 Hz and 0 mA intensity.

Control(Sham) First: Participants will receive sham-control TENS therapy with output setting 0 Hz and 0 mA intensity. The TENS device will be applied at 6 fixed points for 5 minutes each, 1-2 cm

lateral to wound edge and 1-2 cm above along, covering the transverse suprapubic incision. After 4 hours wash out, participants will receive TENS therapy at a frequency of 100 Hz and 5 mA intensity (set at medium pulse width).

At the start of both sessions, TENS at a frequency of 100 Hz and 5 mA intensity will be delivered to the subumbilical region, briefly for 30 seconds only to generate a TENS sensation and enhance the sham. If the sensation cannot be tolerated, participation will be stopped.

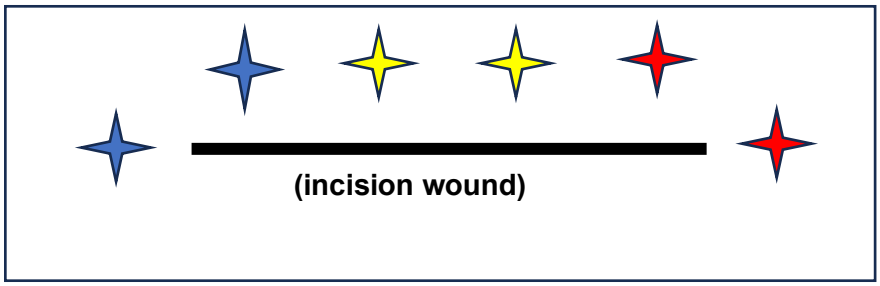
Participants will still receive standard of care analgesics post gynaecology surgery while undergoing the study.



*TENS therapy: frequency of 100 Hz, 5 mA intensity (medium pulse width)
**Control(Sham): frequency of 0 Hz, 0 mA intensity
***TENS: frequency delivered for 30 seconds : frequency of 100Hz, 5 mA intensity

-the devices will be given by provider who are trained by the investigator (they will undergo training on device application and trial process

Prong application points



Data Analysis:

- Data will be entered into SPSS(Version 27, IBM, SPSS Statistics)
- T-test will be used to analyse mean for normally distributed data
- Mann-Whitney U test for non-normally distributed or ordinal data
- Chi-square test (with Fisher exact test if ≥20% of evaluated have expected cell size number <5) for categorical data
- Analysis will be on intention-to-treat basis
- Two-sided p-values were reported and $p<0.0125$ regarded as significant for four primary outcome and $p < 0.05$ for all other analyses

RESEARCH DATA

Where will the data be kept?
The hardcopy data will be kept in a secured locker with a lock in the Obstetric and Gynaecology Department of UMMC. The keys to the lock will be kept by the primary investigator.

Who will have access to the research data?
Only the principal investigators and co-investigators will have access to the research data.

How long will the data be kept?
The data will be kept for 7 years from the last entry.

GANTT CHART

	SEPT 2024-OCT 2024	NOV 2024-AUG 2025	SEPT 2025-FEB 2027	MAR 2027-MAY 2027	JUN 2027-OCT 2027	NOV 2027
PROPOSAL						
ETHICS APPROVAL						
DATA COLLECTION						
DATA ANALYSIS						
THESIS PREPARATION						
SUBMISSION						

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5. Yılmaz, E., Karakaya, E., Baydur, H., & Tekin, I. (Year). Effect of transcutaneous electrical nerve stimulation on postoperative pain and patient satisfaction.

POTENTIAL IMPACT

Evidence of the clinical use of novel TENS in reducing postoperative pain
Practical, low risk adjunct for enhanced recovery protocol
Data may support reduced opioids use

4. Please state whether you have submitted this research proposal for funding, now or before
☐ Yes: If Yes, which grant? _____
☑ No

This proposal will be kept strictly private and confidential. It will not be shared with anyone without your prior approval.

Name of Researcher (CAPITAL): LAVINA A/P BELAYUTHAM

Signature of Researcher: ……

Date: 15th July 2025