

STUDY PROTOCOL

The use of preoperative Virtual Reality to reduce anxiety and pain on gynaecologic patients undergoing surgery

CIRB NUMBER:

2018/2200

PROTOCOL VERSION: 1.0

PROTOCOL DATE: 23 Aug 2018

PRINCIPAL INVESTIGATOR:

A/Prof Sng Ban Leong, Senior Consultant, KK Women's and Children's Hospital (KKH)

*Also refer to Section F8 on the statistical analysis details.

Section A: Protocol Title & Protocol Administrators

A1. Please enter the Full Protocol Title and Protocol Number (if available) for this Study

Protocol Title : The use of preoperative Virtual Reality to reduce anxiety and pain on gynaecologic patients undergoing surgery

Protocol Number (Optional) :

A2. You may assign Protocol Administrators for this study below

No.	Name	Institution/Organization	Department	Office No.	Email
1	Dr Tan Chin Wen	KK Women's and Children's Hospital (KKH)	Department of Women's Anaesthesiology		Tan.Chin.Wen@kkh.com.sg
2	Ms Teo Pei Chih Agnes	KK Women's and Children's Hospital (KKH)	Department of Women's Anaesthesiology		Agnes.Teo.PC@kkh.com.sg
3	Ms Truong Thi Thu Ha	KK Women's and Children's Hospital (KKH)	Department of Women's Anaesthesiology	6576798	ha.truong@sgh.com.sg

Section B: Study Sites, Study Team & Submission Board

B1. Please select the study sites

(i) SingHealth and Partner Institutions: KK Women's and Children's Hospital (KKH)

B2. Study Team Members

	Name	Study Role	Department	Institution/Organization	Designation
1	Dr Sng Ban Leong	PI	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant
2	Mr Goh Zhaohan	Co-I	Office of Clinical , Academic & Faculty Affairs	Duke-NUS	Student
3	Ms Chia Xintian	Co-I	Research Operations	Duke-NUS	Medical Student
4	Dr Chan Ju In Jason	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Resident
5	Dr Goy Wee Lip Raymond	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant
6	Dr Ithnin Farida Binte	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant
7	Dr Mathur Deepak	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant
8	Ms Liu Juan	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	clinical research coordinator
9	Ms Kee Hwei Min	Co-I	Division of Nursing	KK Women's and Children's Hospital (KKH)	NC, APN (Anaesthesia)
10	Ms Xu XueLian	Co-I	Division of Nursing	KK Women's and Children's Hospital (KKH)	Advanced Practice Nurse

B3. Submission Board and other IRB

(i) Which CIRB is this application being submitted to?

CIRB DAnaesthesia (including acupuncture)

(ii) Has the study been submitted to another IRB? No

(iii) Has the application been previously rejected by any IRB? No

Section C: Conflict of Interest

Does the Principal Investigator or any Study Team Member have any potential conflict of interest? The Declaration is also for the immediate family members of the Principal Investigator and Study Team listed below. €

Name	Study Role	Yes/No
Dr Sng Ban Leong	PI	<input type="radio"/> Yes <input checked="" type="radio"/> No
Mr Goh Zhaohan	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Ms Chia Xintian	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Dr Chan Ju In Jason	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Dr Goy Wee Lip Raymond	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Dr Ithnin Farida Binte	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Dr Mathur Deepak	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Ms Liu Juan	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Ms Kee Hwei Min	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No
Ms Xu XueLian	Co-I	<input type="radio"/> Yes <input checked="" type="radio"/> No

Submission Date: 21-Jul-2018

Section D: Nature of Research

D1. Please select one category that best describes your research activities. Clinical Research

D2. Is this a US FDA IND/IDE study or data is intended to be reported to FDA in support of an IND/IDE Application? No

Section E: Study Funding Information

E1. Please give information regarding the study's funding source or sponsor information.

- i. **Name of Grant Agency:** Anaesthesiology ACP
- ii. **Grant Name:** Anaesthesiology ACP Clinical Innovation Support Programme Grant
- iii. **Amount:** 10000
- iv. **Deadline of Grant Application:** 30 September 2017
- v. **Has the grant been approved?** Yes
- vi. **Grant Reference Number** 12/FY2018/P1/06-A21

E2. Who will be responsible for the payment and compensation of injury or illness to participants arising from participation in the study?

The Hospital does not make any provisions to compensate study participants for research related injury. However, compensation may be considered on a case-by-case basis for unexpected injuries due to nonnegligent causes.

E3. Who will be responsible for research-related costs?

Anaesthesiology ACP Clinical Innovation Support Programme Grant

Section F: Research Methodology

F1. Please provide an abstract of your proposed research (Up to 300 words).

In the perioperative setting, distraction therapies have been used as a technique to reduce anxiety and pain in the perioperative period. Measures employed in the local restructured hospitals include television, magazines, and newspapers. Tablet-based activity, music and video distraction therapy have also been shown to be useful to reduce preoperative anxiety. We propose a prospective study to implement and evaluate the use of Virtual Reality (VR) in decreasing in anxiety and pain undergoing gynaecological surgery.

We will administer VR in 100 female adults undergoing day surgery or same-day-admission gynecologic surgery in KKH. The VR will be administered using a Samsung Gear VR3 headset fitted with a smartphone. VR images and sound with calming effect will be delivered to the patients for a short duration of about 10 minutes. This low-intensity activity offers soothing experience to distract the patients from any pain and anxiety.

The use of VR in medical care has shown efficacy in meta-analysis and clinical trials, but has not been implemented in the local context and cultural settings. As a highly interactive and flexible technology, VR is a promising method for anxiety and pain distraction that could be extended for hospital use (rehabilitation, outpatient procedures, diagnostic scanning and perioperative period) as well as all other SingHealth Anaesthesiology Academic Clinical Programme (ACP) sites. This strategy will increase patient satisfaction while providing non-pharmacological anxiolytic effects with no side effects.

F2. What are the specific aims and hypothesis of this study?

- To evaluate the effectiveness of Virtual Reality in reducing patient's hospital and surgery-related anxiety, decreasing pain and analgesic use, increase patient satisfaction and improve patients' recovery;
- To identify the best duration and type of VR exposure for patients;
- To recommend protocol for implementation and operational readiness in all SingHealth Anaesthesiology Academic Clinical Programme (ACP) sites.

F3. Please briefly describe the background to the current study proposal. Critically evaluate the existing knowledge and specifically identify the gap that the proposed study is intended to fill.

Studies have shown that the majority of patients undergoing selective surgery experience different levels of anxiety [1-4]. The degree of anxiety is influenced by factors such as patient demographic characteristics, type of surgery, previous experiences with operational procedures, willingness to undergo the proposed intervention, perceived rapport with hospital personnel and personal stress threshold [2-5]. This anxiety has been shown to be correlated with acute postoperative pain and chronic postsurgical pain, which leads to an increased use of postoperative analgesic, slow recovery [6-8], and other maladaptation behaviours in paediatric patient like eating disorders [9-11]. The link between greater preoperative anxiety and the risk for developing chronic postsurgical pain has been documented in a variety of surgical procedures, including elective abdominal hysterectomy, radical mastectomy, breast cancer surgery, and arthroscopic knee surgery [12-15]. While pharmacological interventions such as opioid-based analgesic are available, other methods to manage anxiety and distract patients from stressors – such as music, television, and virtual reality - have become more popular in the recent years due to their safety, low cost and effectiveness in improving overall patient experience and outcome [16-20].

Virtual reality (VR) is a promising new technology that offers opportunities to modulate pain experience and cognition. Patients received VR treatment reported a reduction in pain and anxiety [21], faster wound healing [22], decreased chronic pain intensity [23] and other neurohabilitation improvements [24]. The recent advent of inexpensive consumer VR system has also made VR more accessible to the mass, especially those by Samsung available locally. In SingHealth, VR has been used in neurosurgery for individualized surgery planning for patients with brain tumours, vascular malfunction and skull based tumours [25]. However, there has been little done to investigate the effectiveness of VR during the preoperative period especially in local setting. Therefore, we will investigate the feasibility and practicability of employing VR in anxiety and pain management in patients undergoing same day admission or day surgery. The proposed intervention may not only be implemented in the preoperative environment but also be in other settings such as before diagnostic screening or minor treatments done during inpatient stay or outpatient visit. The use of VR is suitable for those who are preparing for procedures in clinic or ward as an alternative anxiety management without prolonging the preparation time. The innovation may also be expanded to a larger cohort of patients in all ANAES sites including both adult and paediatric population.

F4. Please provide a list of relevant references.

1. Badner NH, Nielson WR, Munk S, Kwiatkowska C, Gelb AW. Preoperative anxiety: detection and contributing factors. *Can J Anaesth.* 1990; 37: 444 -7
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5. Millar K, Jelacic M, Bonke B, Asbury AJ. Assessment of preoperative anxiety: comparison of measures in patients awaiting surgery for breast cancer. *Br J Anaesth*. 1995; 74(2): 180-3
6. Suffeda A, Meissner W, Rosendahl J, Guntinas-Luchius O. Influence of depression, catastrophizing, anxiety, and resilience on postoperative pain at the first day after otolaryngological surgery: A prospective single center cohort observational study. *Medicine*. 2016; 95 (28): e4256
7. Pinto PR, McIntyre T, Nogueira-Silva C. Risk factors for persistent postsurgical pain in women undergoing hysterectomy due to benign causes: a prospective predictive study. *J Pain*. 2012; 13:1045-1057
8. Gerbershagen HJ, Dagtekin O, RÖthe T. Risk factors for acute and chronic postoperative pain in patients with benign and malignant renal disease after nephrectomy. *Eur J Pain*. 2009; 13:853-860
9. Kain ZN, Mayes LC, Caldwell-Andrew AA, Karas DE, McClain BC. Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. *Pediatr*. 2006; 118:6518
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11. McCann ME, Kain ZN. The management of preoperative anxiety in children: an update. *Anesth Analg*. 2001; 93:98-105
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14. Katz J, Poleshuck EL, Andrus CH. Risk factors for acute pain and its persistence following breast cancer surgery. *Pain*. 2005; 119:16-25
15. Robertson A, Khan R, Fick D, Robertson W B, Gunaratne DGR, Yapa S, Bowden V, Hoffman H, Rajan R. The effect of virtual reality in reducing preoperative anxiety in patients prior to arthroscopic knee surgery: A randomized controlled trial. 2017 IEEE 5th International Conference on Serious Games and Applications for Health (SeGAH), Perth, WA, 2017, pp. 1-7.
16. Wang S, Kulkarni L, Dolev J, Kain Z. Music and preoperative anxiety: A randomized controlled study. *Anesthesia and Analgesia* 2002; 94:1489-94
17. Lechtzin N, Busse AM, Smith MT, Grossman S, Nesbit S, Diette GB. A randomized trial of nature scenery and sounds versus urban scenery and sounds to reduce pain in adults undergoing bone marrow aspirate and biopsy. *J Altern Complement Med*. 2010; 16:965-972.
18. Dascal J, Reid M, Ishak WW, Spiegel B, Recacho J, Rosen B and Danovitch I. Virtual reality and medical inpatients: a systemic review of randomized and controlled trials. *Innov Clin Neurosci*. 2017. 14(1-2): 14-21.
19. Seiden, S. C., McMullan, S., Sequera-Ramos, L., De Oliveira, G. S., Roth, A., Rosenblatt, A., Jesdale, B. M. and Suresh, S. Tablet-based Interactive Distraction (TBID) vs oral midazolam to minimize perioperative anxiety in pediatric patients: a noninferiority randomized trial. *Paediatr Anaesth*. 2014; 24: 1217–1223. doi:10.1111/pan.12475
20. Tashjian VC, Mosadeghi S, Howard AR, Lopez M, Dupuy T, Reid M, Martinez B, Ahmed S, Dailey F, Robbins K, Rosen B, Fuller G, Danovitch I, IsHak W, Spiegel B. Virtual Reality

21. Jeffs D, Dorman D, Brown S, Files A, Graves T, Krik E, Meredith-Neve S, Sanders J, White B, Swearingen CJ. Effects of virtual reality on adolescent pain during burn wound care. J Burn Care Res. 2014, 35:395-408
22. Brown NJ, Kimble RM, Rodger S, Ware RS, Cuttle L. Play and heal: Randomized controlled trial of Ditto intervention efficacy on improving re-epithelialization in pediatric burns. Burns. 2014, 40:204-213
23. Sato K, Fukumori S, Matsusaki T, Maruo T, Ishakawa S, Nishie H, Takata K, Mizuhara H, Mizobuchi S, Nakatsuka H. Nonimmersive virtual reality mirror visual feedback therapy and its application for the treatment of complex regional pain syndrome: An open-label pilot study. Pain Med. 2010, 11:622-629
24. Wang M, Reid D. Virtual reality in pediatric neurohabilitation: Attention deficit hyperactivity disorder, autism and cerebral palsy. Neuroepidem 2011, 36:2-18
25. SingHealth Virtual Reality Neurosurgery. Accessed on 07 Sept 2017 at <https://www.singhealth.com.sg/PatientCare/Overseas-Referral/En/Procedures/Pages/Virtual-RealityNeurosurgery.aspx>

F5. Please provide an account of the Principal Investigator's preliminary studies and progress reports (if any) pertinent to this application.

Not applicable.

F6. Please state concisely the importance of the research described in this application by relating the specific aims to the long term objectives.

1. **Access for patients:** Commercially available Virtual Reality headsets like Samsung Gear VR3 has recently become easily accessible to the public. The headset is inexpensive, highly portable, lightweight and easy to use, making it ideal for users to create their individual virtual reality experience for pain and anxiety relief anytime with little side effects.
2. **Patient experience and satisfaction:** Patient satisfaction is an important indicator of the outcome of pain management and evaluation of the quality of services in healthcare. Unlike pre-scheduled preoperative visit or inpatient surgery, same day surgery and same day admission surgery provides a limited amount of time available for the anesthesiologist to address the psychological aspect of pain management in patients. Thus, the use of Virtual Reality is to provide enjoyable and calming experience to patients and ultimately increases their satisfaction during the perioperative period.
3. **Pursuit of care improvements through research and innovation:** We aim to create a compassionate, individualized and effective approach to deliver care to patients. That can be done in this project by taking advantage of the latest advance in consumer-focused technology. It is also part of the greater paradigm shift in which non-pharmacological and noninvasive methods are becoming more common to treat patients and enhance their experience. There is potential to enable the patients to take the autonomy of home care by showing them a possibility of reducing anxiety and pain in the inpatient and outpatient settings.

F7. Discuss in detail the experimental design and procedures to be used to accomplish the specific aims of the study.

We will conduct a prospective cohort study in 100 female adult subjects that undergo gynecologic surgery (day surgery or same day admission surgery) in KK Women's and Children's Hospital, Singapore. Informed consent will be obtained from all subjects.

Recruitment

Patients who are undergoing gynecologic surgery will receive study information either at pre-operative assessment clinic or upon admission for surgery if they have not attended the pre-operative assessment clinic. They will be screened for eligibility using the inclusion and exclusion criteria. If eligible for recruitment, the patients will be approached by the investigators for recruitment. Once consent is obtained, the recruiter will collect the patient's baseline demographic data.

Procedures

Patient will then be given a Samsung Gear VR3 headset fitted with a smartphone. She will choose the desired playlist on calming scenario and experience the VR for about 10 minutes, seated in a quiet environment in pre-operative waiting area before her turn for the scheduled surgery. Patient will be asked on their satisfaction on the VR experience after the intervention. Hospital Anxiety and Depression Scale (HADS), Spielberger State-Trait Anxiety Inventory (STAI) and EQ-5D-3L questionnaires will be conducted during this period.

During and after the gynecologic surgery, baseline demographic data, analgesia usage and monitoring as per standard care will be recorded. Patient will be sent to the recovery room after the surgery, and the study team members will collect their Pain score, Hospital Anxiety and Depression Scale (HADS) and EQ5D-3L.

All the headsets will be disinfected following the hospital's infection control guideline.

Outcome

Primary outcome: Pain score, Hospital Anxiety and Depression Scale (HADS) score, EQ-5D-3L, and Spielberger State-Trait Anxiety Inventory (STAI) score.

Secondary outcome: Analgesia usage, patient's satisfaction with the use of VR.

Duration of study

The study will be conducted upon their admission to day surgery (visit 1) and will be conducted again when they are sent to recovery room (visit 2). The whole study duration may take about 1 day.

F8. Please provide details on sample size and power calculation and the means by which data will be analyzed and interpreted (if applicable).

This is a pilot prospective cohort study and therefore no sample size calculation is made available. In order to assess the feasibility of virtual reality to relieve pain in KKH, and therefore 100 adult female subjects that undergo gynecologic surgery will be needed. Paired t – tests and McNemar' test for paired data were used for continuous and categorical data.

F9. List all activities that are carried out as part of research in this study. Please state/list all procedures involved in this research study and attach the data collection form (if any) which will be used for CIRB review.

Before surgery:

- Patient recruitment before the surgery
- Baseline Demographic data collection
- Selection of calming scenario by patient
- VR experience for ~ 10 minutes via headset fitted with a smartphone
- Data collection (pain score, HADS score, EQ-5D-3L, STAI, patient's satisfaction)

After surgery:

- Survey and data collection (pain score, HADS score, EQ-5D-3L, analgesia usage)

F10. Please describe the participant's visits (frequency and procedures involved).**Visit 1:**

Patients who are undergoing gynecologic surgery will receive study information either at pre-operative assessment clinic or upon admission for surgery if they have not attended the pre-operative assessment clinic. They will be screened for eligibility using the inclusion and exclusion criteria. If eligible for recruitment, the patients will be approached by the investigators for recruitment. Once recruited, the patient will be given device for virtual reality experience for about 10 minutes. Pain score, Hospital Anxiety and Depression Scale (HADS) score, STAI, EQ-5D-3L questionnaire and patient satisfaction on the VR experience will be conducted during this period.

Visit 2:

Before patient is discharged from recovery room, pain score, HADS score and EQ-5D-3L will be collected, which will take about 10 minutes. The use of pain medication will also be recorded.

F11. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims.

One potential challenge to this study is to have a suitable list of calming scenarios for study participants.

While the therapeutic effect of VR has been studied in other countries, data for such research in Singapore is not widely available. Also, Singapore being a multi-racial and multi-cultural country would mean that the study subjects could come from different ethnic background and thus potentially will have a wide range of preferences.

F12. What are the potential risks to participants?

Virtual reality sickness may occur when a person's exposure to a virtual environment causes symptoms that are similar to motion sickness symptoms. The most common symptoms are general discomfort, headache, stomach awareness, nausea, vomiting, sweating, fatigue, drowsiness, disorientation, and apathy. Other symptoms include postural instability and retching. To avoid the possible risks, the recommended time for the VR experience is limited only to 10 minutes (which is far below from the 30 minutes that the device manufacturers usually recommend), and that the use of VR may only take place in private settings (quiet room or waiting area) so as to allow the patient to stay aware of the people, objects, and architecture around them.

No new research medications are involved by joining the study. The drugs being delivered are the same as what the patient shall receive as standard care.

F13. What are the potential benefits (direct as well as indirect) to participants? Indirect benefit may refer to the medical knowledge gained in the future, from the research.

The potential direct benefits to participants are that their anxiety may be reduced before surgery. Those having high level of anxiety in recovery unit will be advised to seek clinical psychiatric assessment at KK Hospital. It is also possible that post-op pain and analgesia usage may be reduced, leading to a better patient outcome and satisfaction. One indirect benefit to the patient is the satisfaction of helping the society to source for a convenient and less costly pain relief option. Patients' participation in this study may help us to confirm the protocol so as to implement the use of VR as a non-invasive pain relief intervention in perioperative setting, which may further expand to other healthcare institutions in Singapore.

Section G: Recruitment Details

G1. How will potential participants be identified? Please tick all the applicable boxes.

- Referral by attending healthcare professional
- Patients of study team
- Databases
- Other methods of participant identification

G2. Who will make the first contact with participant?

Principal Investigators or the Co-Investigators will make the first contact with participant.

G3. How will the participant be contacted?

Patients who are undergoing elective surgery will receive study information either at pre-operative assessment clinic or upon admission for surgery if they have not attended the pre-operative assessment clinic. They will be screened for eligibility using the inclusion and exclusion criteria. If eligible for recruitment, the patients will be approached by the investigators for recruitment. Recruitment will be performed in the pre-operative assessment clinic or on the same day of surgery if they have not attended pre-operative assessment clinic. Research personnel will conduct all discussions about the study and answer any questions in a private manner in the consultation rooms. They will be counselled regarding the alternatives and given an opportunity to ask questions and clarify doubts. Ample time will be given to the potential patients for consent taking. Consent will be obtained in writing upon their willingness and agreement to participate in the study.

G4. Will any advertising/recruitment materials be used to recruit research participants?

Yes

- II Brochures

Please state the location(s) where the brochures will be placed (e.g. in the general waiting area in Clinic X), and attach a copy of the brochure. In the pre-admission clinics.

G5. Will any other recruitment strategies be used (e.g. talks in public places, societies etc.)?

No

G6. What is the Recruitment Period (if applicable)? Please provide us with the approximate recruitment period.

Start Date: 02-Apr-2018

End Date: 01-Apr-2020

If this is a Medical Record Reviews, please indicate the period of the data that will be extracted for review.

G7. How long will the participants be directly involved in the study (if applicable)? This includes the time from the screening procedures till completion of follow-up tests or examinations.

Patients will be involved in the study during their hospitalization stay, i.e. from the time just before surgery until the patient is discharged from the post-operative observation area. This will take about 1 day.

Section H: Study Sites & Recruitment Targets

H1. Please state the target number of research participants to be recruited for each study site in Singapore.

No.	Study Site	Total Recruitment Target	Adults (Male)	Adults (Female)	Children
1	KK Women's and Children's Hospital (KKH)	100	0	100	0

H2. Is this study part of an international study?

No

Section I: Research Participant Characteristics

I1. Please list the inclusion criteria for research participants in this study.

- Healthy participants who are ASA 1 and 2 (with well-controlled medical problems);
- Undergo day surgery or same-day-admission gynecologic surgery;
- No visual impairment.

I2. Please list the exclusion criteria for research participants in this study.

- Patients with significant respiratory disease and obstructive sleep apnea;
- Patients who are unable to understand the questionnaires;
- Obstetric patients
- Motion sickness in 3D environment

I3. Please state the age group of the research participants.

Lower Age limit 21

Upper Age limit 70

Submission Date: 21-Jul-2018

14. Are there any recruitment restrictions based on the gender of the research participants (e.g. only males will be included in this study)?

Yes. Only females undergoing gynecologic surgery in KKH will be recruited.

15. Are there any recruitment restrictions based on the race of the research participants (e.g. only Chinese participants will be included in this study)?

No

16. Do the potential research participants have a dependent relationship with the study team (e.g. doctor-patient, employee-employer, head-subordinate, student-teacher, departmental staff relationship)?

No

17. Does the study involve any vulnerable research participants? Please select 'Yes' to view the options and select the applicable population(s).

No

18. Does the study involve any of the following?

Inpatients.

Outpatients.

Healthy Volunteers.

Not applicable.

Section J: Consent Process – Consent Required

J1. Describe when the consent process will take place with the potential participant.

Participants should be approached prior to the initiation of any study procedures and should not be approached in a situation where they may feel compromised (e.g. while in labour, just prior to a surgical procedure or under sedation).

Patients will be approached in the preoperative clinic or wards. The Investigator will explain to the patients about the study and patients will be given time to read about the study before obtaining their consent. Adequate time will be given for patients' consideration of participation and discussion with the investigators to clarify any doubts. With the activation of HBRA, informed consent will be obtained in the presence of a prescribed witness.

J2. Where will the consent process take place with the potential participant (e.g. in room ward, outpatient clinic etc.)? Please justify why the place chosen for the consent process is suitable.

Informed consent will be taken place in the preoperative clinic consultation room or wards in a private manner.

J3. Please describe the consent process as follows:

i. Explain if adequate time will be given to the participant to consider their participation.

Patients will be approached in the preoperative clinic or wards and will be explained and given time to read about the study before obtaining their consent.

ii. Please explain if the place where consent will be taken is suitable. This place should allow the participants to be comfortable and have the right frame of mind to consider participation. Patients will be approached in the preoperative clinic or wards and will be explained and given time to read about the study before obtaining their consent.

iii. Please explain how the person taking consent would minimise the possibility of coercion or undue influence.

Study participants will receive a patient information sheet. This will be discussed with them in private in the preoperative clinic consultation room or wards (private room). The subjects are able to withdraw from the study at any point. The contact details of the Principal Investigator will be provided in the information sheet.

J4. Does your study involve potential vulnerable participants whereby obtaining informed consent from the participant is not possible and informed consent is required from a Legal Representative (LR)?

No

J5. Please describe the provisions to protect the "privacy interest" of the participants (e.g. consent will be obtained in a separate room, free from intrusion and participants are comfortable with the proposed settings).

Research personnel will conduct all the discussions about the study and answer any question in private manner.

J6. Will consent be documented in the form of a written and signed Research Participant Information Sheet and Consent Form?

Yes

File Name	Description	Version Number	Version Date
PIS VR Ver 3 (tracked changes).doc	VR PIS V3 (tracked changes)	3	25Apr2018
PIS VR Ver 3 (clean copy).doc	VR PIS V3 (clean copy)	3	25Apr2018

J7. Will research participants receive any monetary payments (including transportation allowances) or gifts for their participation in the study?

No

J8. Besides the Informed Consent Form, will any other materials or documents be used to explain the study to potential Research Participants (e.g. scripts, hand outs, brochures, videos, logs etc.)?

No

J9. Will the study enrol non-English speaking participants?

No

J10. Will the study be recruiting participants under emergency situations, when prior consent of the participant is not possible, and the consent of the participant's legal representative, if present, should be requested?

No

J11. Do you have any additional comments regarding the Informed Consent process?

No

Section K: Research Data Confidentiality

K1. Will coded/anonymous research data be sent to the study sponsor (e.g. pharmaceuticalsponsored studies)?

No, the study team would store all research data within the institution.

i. Please state where the research data (soft copy and/or hardcopy) will be stored and indicate if the location storage is secured (i.e Password Protected PC or Laptop, data stored in physical location with lock and key access.)

The soft copy of research data will be stored in a password protected PC. Hard copies of data collection forms are kept by the Principal Investigator under lock and key. The data is accessible only by Investigators for analysis purposes only.

ii. Who will have access to the research data, and how will access to the research data be controlled and monitored? (Please state the personnel who will have access to the study data eg.

Principal Investigator, Co-Investigator, study coordinator.)

The Principal investigator and co-investigators. The research data will be locked and soft copy will be under the computer security of SingHealth.

iii. Are there any other measures in place to protect the confidentiality of the research data? No names or identification number that will identify subjects will be ensured. The subjects are only identified by study number.

iv. Are there any research data sharing agreements with individuals or entities outside the Institution, to release and share research data collected?

No

v. Describe what will happen to the research data when the study is completed.

The research data will be kept under lock and key and using computer security of Singhealth. The data will be destroyed after keeping for 6 years upon completion of the study.

K2. Will any part of the study procedures be recorded on audiotape, film/video, or other electronic medium?

No

Section L: Data & Safety Monitoring

L1. The purpose of the Data and Safety Monitoring Plan is to ensure the safety and well-being of participants, and the integrity of the data collected for the study. Depending on the type and risk level of the study, this may include the Principal Investigator, experts within the department or institution, independent consultants or a combination of the said persons.

Who will perform the data and safety monitoring?

The data is kept by the principal investigator under lock and key and using computer security of SingHealth. The data is accessible only by the investigators for analysis purposes only. The plan for adverse effect monitoring would include reporting to CIRB.

L2. Please describe the frequency of review (e.g. daily, weekly, quarterly) and what data (e.g. adverse events/serious adverse events) will be monitored for safety.

Safety data is monitored at all times by the investigators. There will be monthly meetings to review the trial.

Adverse events and serious adverse events will be reported to CIRB accordingly.

L3. How is data integrity monitored to ensure that study data is authentic, accurate and complete, and if the data correlates with the case report forms?

Data is extracted from data collection forms and random audits will be performed to make sure it is authentic, accurate and complete.

L4. Please describe the stopping criteria for the research study based on efficacy, futility and safety criteria.

The stopping criteria for the research study will be based on safety criteria. The review of serious adverse effects will be performed.

L5. Please state the route of dissemination of any data and safety information to the study sites, as well as the person/team responsible for doing so.

Face-to-face communication and email correspondence.