Influence of Anesthetic Technique on Acute and Chronic Neuropathic Pain

ClinicalTrials.gov Identifier: NCT02527083

Study Protocol and Statistical Analysis Plan

Document Date: 5/22/2017

VA Pittsburgh Healthcare System

ProSPECT - Protocol Submission Portal and Electronic Communication Tracker

Date: Monday, May 3, 2021 1:30:26 PM

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ID: Pro00000878 View: 0.0 Type of Submission Entry

Study Identification Information

This is the first step in your Human Research Application. You will automatically be guided to the appropriate forms needed to complete your submissions.

1.0 * **Study Name:**
Influence of Anesthetic Technique on Acute and Chronic Neuropathic Pain

2.0 * **Brief Description (using layman's terms) - 500 words or less:**
Research suggests that the type of anesthesia used for surgery may affect intraoperative stress hormone levels. There is also data to support that an increased level of stress hormones leads to increased pain after surgery. The primary aim of this study is to determine the effect of anesthesia type on long term pain after hernia surgery. In this study, patients undergoing inguinal hernia repair will be randomized to an anesthetic group, either Total Intravenous Anesthesia (TIVA) maintained with propofol or Balanced Inhaled Anesthesia (BIA) maintained with sevofluorane. Four different subjective pain scales will be given as oral or written surveys at various time points after surgery in the acute period (prior to Post Anesthesia Care Unit discharge, 24 hours, and 1 month after surgery) and chronic period (3, 6, and 12 months after surgery). This will allow us to look at any differences in short and long-term pain after hernia repair depending on type of anesthesia received.

3.0 * **Is this research study a Greater than Minimal Risk Clinical Trial?** ◉ **Yes** ○ No

4.0 * **Is this study a Greater than Minimal Risk Comparative Effectiveness research?** ○ Yes ◉ **No**

5.0 * **Principal Investigator:**
James Ibinson

5.1 * **VA hours per week the PI is devoted to project:**
5

5.2 * **Is the PI working with ionizing radiation?** ○ Yes ◉ **No**

5.3 * **Is the PI working with biological hazards?** ○ Yes ◉ **No**

5.4 * **Is the PI shipping biological hazards?** ○ Yes ◉ **No**

A completed and signed Research Financial Conflict of Interest Statement is required for all investigators (including Principal Investigators, Co-Principal Investigators, and Co-Investigators) listed on the study application. **Financial Conflict of Interest Form-Nov. 2013**

5.5 **Upload Financial Conflict of Interest Statement:**

6.0 Research Staff:

Researcher	Role in Project	Hours per Week devoted to project	Administer Informed Consent	Working with Ionizing Radiation	Working with Biologicial Hazards?	Shipping biological hazards?	FCOI Form
Brian Williams	Co-Investigator	1	no	no	no	no	
Visala Muluk	Co-Investigator	2	no	no	no	no	

7.0 Type of Submission:

Description
(●) **This is a new study. This has not previously been submitted to the IRB.**
( ) This is a new paper conversion. This study has been previously approved by the IRB.

If this is a 'New Paper Conversion' please include the MIRB Number:

Please upload a letter certifying that you have made no modifications or amendments in converting this research study from paper to electronic:

ID: Pro00000878 View: 1.0 Study Identification Information

Study Identification Information (Continued)

1.0 * **Do you certify that all research staff administering informed consent are knowledgeable about the study?**

yes

2.0 * **To the best of your knowledge do you, or any member of your research staff, have any potential, actual or perceived conflict of interest of a professional or personal nature that may affect any aspect of the research, including, but not limited to, the review and/or conduct of this study?**

○ Yes ◉ **No**

If yes, provide a description, including name of study team member with conflict:

3.0 * **Qualifications of the Investigators:**

Dr. Ibinson (PI) is an experienced investigator within the VAPHCS and an anesthesiologist at VAPHS. His research focus is in pain, and he has published extensively on pain-induced brain activity. He is also well-trained in statistics, having contributed to the statistical analysis of numerous publications over the past 5 years.

Dr. Williams is a Professor of Anesthesiology at the University of Pittsburgh. He is the director of Acute Pain Medicine / Regional Anesthesia, Ambulatory Anesthesiology, and the Interdisciplinary Medical Perioperative Assessment Consultation and Treatment (IMPACT) Clinic at VAPHS. He has served as lead author of over 50 publications, including multiple studies surround peri-operative pain.

Dr. Muluk is an Associate Professor and the Director of the Medical Consult Service, and of Primary Care within the IMPACT clinic. She has a played substantial role in the establishment of the IMPACT clinic, including the development and implementation of the Computerized Patient Record System. She is currently the local PI of the BRIDGING study, funded through the NCLBI/NIH.

ID: Pro00000878 View: 1.2 VA Involvement

VA Involvement

1.0 Does the proposed research involve any of the following?:

	Name
☐	VA Funding
☐	VA Personnel Funded Effort
☑	**VA Patients or their Private Health Information**
☐	Other VA Resources: Central IRB
☑	**Other VA Resources: VA Equipment**
☑	**Other VA Resources: VA Property (Including space leased to, or used by VA)**
☑	**Other VA Resources: VA Databases**
☐	None of the Above apply to this research

ID: Pro00000878 View: 1.3 Study Funding Information

Study Funding Information

1.0 * **Funding Sources:**

Funding Source	(Other)	Code
There are no items to display		

2.0 **Upload Grant Application, if applicable (If NIH, VA, voluntary agency, must upload):**

Name	Modified Date
There are no items to display	

ID: Pro00000878 View: 1.4 Resources

1.0 * **Do you currently have adequate resources (e.g., staff, physical space, information technology, etc.) to protect the safety of participants, staff, and the confidentiality of subjects' data during the conduct of this study?**

◉ **Yes** ○ No

If yes, include a listing of the VAPHS resources that will be used for this study and are necessary to protect participants.
Electronic records will be kept in the password protected account on the VAPHS computer server. Paper records will be kept in a locked cabinet in the PI's locked office within the Anesthesiology suite of the VAPHS University drive hospital. Additionally, Katherine Negy, the Education and Outreach Coordinator, will work with me to develop an education plan to assist me in ensuring regulatory requirements are met.

If no, please describe the resources that will be needed and explain how the resources will be obtained before the study is initiated:

2.0 * **VAPHS requires that either the PI or co-PI have a *physical presence* at VAPHS. Please describe the role the PI and/or co-PI have at VAPHS with respect to clinical responsibilities or in relation to other research activities.**
Dr. Ibinson is a practicing anesthesiologist contracted to the VAPHS with clinical responsibilities for 20% of his time. The remaining 80% of his time is dedicated to pain and anesthesia research. He also posesses an WOC agreement for reseach at VAPHS. He is currently present in his office, located in the Anesthesiology suite on the 3rd flood of Building 1, approximately 50% of his academic time. This time can be increased when this study is active.

3.0 * **Will off-site ancillary service facilities (e.g., radiology services, central labs, non VA space, etc) be used for this study?**

○ Yes ◉ **No**

If yes, please provide the location and a brief description of the project activities to be conducted at the off-site ancillary facilities:

4.0 * **Will a firm be contracted to obtain consent from subjects, collect private individually identifiable information from human subjects, or be involved in activities that would institutionally engage the firm in human subjects' research?**

○ Yes ○ No

If yes, please provide a description of the contracted service(s):

* Please specify the IRB that has oversight of the firm's activity(ies):

Name of Site / Institution	IRB Approval Document	FWA Number
There are no items to display		

5.0 **Collaborations**
Please list any non-VAPHS institutions or individuals (i.e. co-authors, mentors, etc.) that you will collaborate with and describe their specific role in the research:

5.1 If this is not Multi-Site Research, please upload the appropriate written agreement(s) here:

Name
There are no items to display

ID: Pro00000878 View: 1.5 Project Information

1.0 Does the project involve any of the following (check all that apply):

	Type
☐	Biological Hazards (including human biological specimens)
☐	Chemicals
☐	Ionizing radiation or use of radioactive materials
☑	**Drug, Biological, or Nutritional (e.g. herbal or dietary) Supplement**

2.0 Project Focus (check if applicable):

	Type
☐	Traumatic Brain Injury (TBI)
☐	Post Traumatic/Post Deployment Stress Disorder (PTSD/PDSD)
☐	Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF)

3.0 KEYWORDS

Please provide a minimum of 3, maximum of 6 keywords. Please use MeSH terms.

* Chronic pain
* Herniorrhaphy
* Stress, Physiological

Anesthetics, General

Intraoperative Period

4.0 * Please describe the type of study:

This will be a randomized, prospective interventional study. Patient care will remain at a level of best practice as no drug or protocol under investigation is experimental.

5.0 * Will any of the research being conducted as a part of this study be used to fulfill academic requirements (e.g., master's thesis, dissertation, or other academic program requirements necessary to obtain a degree/certification, etc.)? ○ Yes ◉ **No**

ID: Pro00000878 View: 1.6 Study Locations

Study Locations

1.0 * **Please add the local sites where this study will be conducted:**

Location

View VAPHS University Drive Division

If Other, Please Specify:

2.0 * **Is this a multi-site study:**

○ Yes ◉ **No**

ID: Pro00000878 View: 1.7 Section Chief and Service Line VP approvals

Please upload the approval of the Section Chief, if applicable and the Service Line VP.

1.0 * **Institutional Approval Document:**
Ibinson Inst Approval.pdf(0.01)

ID: Pro00000878 View: 2 Study Objectives & Design

Study Summary

1.0 Funding End Date:

2.0 * **Abstract. Please provide a brief description of the study**.

The objective of this study is to determine if incidence of chronic neuropathic pain (CNP) varies as a function of anesthetic technique in patients undergoing inguinal herniorrhaphy surgery at VAPHS, hypothesizing that a total intravenous anesthetic (TIVA) protocol utilizing propofol and lidocaine will result in a lower incidence of acute and chronic neuropathic pain (ANP and CNP, respectively) than an inhalational anesthetic based protocol.

This is a patient-blinded, prospective, randomized study. Forty-eight patients undergoing either inguinal (including femoral) or ventral (including umbilical) herniorraphy that requires general anesthesia in the operating room will be enrolled. Exclusion criteria include: those unable to communicate directly with the investigators, a history of disease that prevents anesthetic randomization, the presence of any pain-related disorders such as fibromyalgia, and the need for emergency surgery. Patients will be assigned to one of three anesthetic technique protocols: TIVA with ketamine (TIVA-K), TIVA with remifentanil (TIVA-R), or Balanced Inhalational Anesthesia (BIA, consisting of an inhanale$ anesthestic only) using a computer-generated random numbers table. Sixteen subjects will be used in each group.

The medications administered in the operative room will be recorded. Study data will include the pain numerical rating scale (NRS, the traditional 0-10 pain score where 0 indicts no pain and 10 equates to the most intense pain imaginable) at rest and with movement, the revised version of the short form McGill Pain Questionnaire (sf-MPQ), the self-report of the Leeds Assessment of Neuropathic Symptoms & Signs (s-LANSS), and the Pain Quality Assessment Scale (PQAS). These will be collected during the pre-operative assessment, in the PACU prior to discharge, approximately 24 hours post-operative, 1 months post-operative, 3 months post-operative, 6 months post-operative, and 12 months post-operative.

3.0 * **Describe the study objectives. Please include primary aim and hypothesis, if applicable any secondary aims and hypotheses.**

Objective and Specific Aims

To determine if incidence of chronic neuropathic pain (CNP) varies as a function of anesthetic technique in patients undergoing inguinal herniorrhaphy surgery at VAPHS.

Primary Aim

Total intravenous anesthesia (TIVA) and balanced inhaled anesthesia (BIA) are current techniques used nearly interchangeably for the maintenance of anesthesia during various surgical procedures, including herniorrhaphy surgery. Research evidence supports that reduced intraoperative stress hormone levels result from the use of TIVA versus BIA. There is also data to support that an increased level of intraoperative stress hormones leads to an increased pain score postoperatively. The primary aim of this study is to determine the effect of TIVA versus BIA in the incidence of CNP following herniorraphy surgery. No studies currently exist in the literature demonstrating a link between physician-selected general anesthetic technique and the incidence of CNP.

Hypothesi(e)s

In patients undergoing herniorrhaphy, a TIVA anesthetic protocol will result in a lower incidence of acute and chronic neuropathic pain (ANP and CNP, respectively) than a BIA anesthetic protocol.

Secondary Aims

For each anesthetic protocol: [i] the proportion of patients experiencing ANP; [ii] the proportion of ANP patients developing and not developing CNP; [iii] the rate of CNP given ANP; [iv] and a comparative analysis of the postoperative pain scores will also be performed, testing the link between anesthetic technique and acute pain, as well as ANP's connection to CNP. Additionally, data regarding the intraoperative stress response will be collected in an attempt to replicate the findings that TIVA results in lower intraoperative stress levels than BIA.

4.0 * Provide a summary of the background of the study, and explain how this research will contribute to existing knowledge. Describe previous studies that provides a basis to show that the proposed research can be carried out without undue risk to human subjects.

It has long been known that chronic pain is a common negative outcome following hernia repair and its sufferers often frequent pain clinics. Estimates of the incidence of chronic pain following herniorraphy range from 10%(1) to as high as 63% at 12 months after surgery.(2) Despite the improved immediate pain outcomes with laparoscopic techniques, a chronic pain incidence of 15% has been found at 9 months after the procedure.(3) CNP causes a burden to the patient and the healthcare system. In a study of thoracic surgery, Searle et al demonstrated that ANP is predictive of CNP with a 3.5 times increased relative risk in patients who experience ANP in the postoperative period, as measured by the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale. However, ANP is not the only factor that determines CNP as demonstrated in the same study of thoracic surgery in which 8% of patients developed ANP while a far greater 22% experience CNP at 3 months(4).

The factors predisposing a patient to CNP may begin even before incision. The body mounts a stress response in reaction to perioperative surgical noxious stimulation including but not limited to intubation, incision, maximum surgical stimulation, and extubation with activation of the sympathetic nervous system and release of stress hormones including epinephrine, norepinephrine, cortisol, and ACTH.(5) The goal of anesthesia and analgesia is to reduce this stress response and suppress pain pathways. However, choice of anesthetic may influence intraoperative stress response with increased sympathetic outflow seen when using balanced inhaled anesthesia (BIA) maintained with sevoflurane versus a total intravenous anesthetic maintained with propofol (TIVA).(6) The use of perioperative intravenous ketamine and lidocaine are other anesthetic modifications demonstrating an attenuated surgical stress response with smaller increases in heart rate and blood pressure as well as decreased plasma cortisol levels.(7)

Studies have shown that increased intraoperative stress hormone activation is related to increased pain perception in the postoperative period.(8) If intraoperative stress hormone activation can be attenuated by anesthetic technique, it would provide support for an existing standard of care method to reduce acute and chronic neuropathic pain in postoperative patients.

5.0 * Describe the overall significance of the research in terms of the problem to be studied and potential findings, as well as its relevance to the care of veterans, the VAPHS, and the VHA:

With an incidence of up to 63% of patients developing CNP following herniorraphy surgery(2), it is imperative that medical speciality of anesthesiology investigates changes that can be made to

technique to reduce the intraoperative stress experienced by the patient and thus the possible development of acute and chronic neuropathic pain. This study will help to determine the correlation between anesthetic technique and CNP with herniorraphy surgery. It may improve control of acute postoperative pain leading to decreased incidence of CNP.

This issue is extremely relevant to the VHA, and the VAPHCS, which has a large volume of herniorraphy surgical patients and a high burden on the system of patients with refractory chronic pain seeking treatment in the pain clinic.

6.0 Please upload any additional documents:

Name	Version
There are no items to display	

ID: Pro00000878 View: 2.1 Required Reviews

Required Reviews

1.0 **Type of Submission:**

New study

If this is a 'New Paper Conversion' please include the MIRB Number:

Please upload a letter certifying that you have made no modifications or amendments in converting this research study from paper to electronic:

2.0 * **Requested Review Type:**

Name	
○	Exempt
○	Expedited
◉	**Full IRB Review**
○	Not Human Subject Research

3.0

	Please check which of the following Service Lines/Departments/Entities will be impacted or used in the conduct of this study	**Upload Letter of Support**
☐	Clinical Support	
☐	Medical Specialty	
☐	Investigational Drug Service	
☐	Imaging	
☐	Community Based Care	
☐	Patient Care Services	
☐	Behavioral Health	
☐	Primary Care	
☑	Surgical Specialty	Ibinson Surg Service Line Support.pdf(0.01)
☐	Critical Care	
☐	Clinical Trials Center	
	☐ Regulatory Coordinator Support Core	
	☐ Clinical Coordinator Support Core	
	☐ Ancillary Support Core	
	☐ Data Support Core	
☐	Research Registry Registry Number:	
☐	Other	

If Other, please specify:

ID: Pro00000878 View: 3 Research Design

Methods & Procedures

1.0

* **Does this research study involve any of the following:**

Name	
☐	Deception
☐	Interview/Focus Groups
☑	**Use of Drug, biological, or nutritional (e.g., herbal or dietary) supplement (investigational or FDA approved)?**
☐	Use of medical devices
☐	Prospective Analysis of Specimens
☐	Banking of Specimens-Data
☐	Retrospective use of specimens
☐	Audio/Video Recordings or Photographs
☐	Honest Broker or other similar service
☐	None of the Above

ID: Pro00000878 View: 3.3 Drug, Biological, or Nutritional Supplement

Drug, Biological, or Nutritional (e.g., herbal or dietary) Supplement

1.0 * **List all drugs on this study:**

Generic Name	VA Class	Other	Manufacturer of Drug	IND Holder	IND Number
REMIFENTANIL	CN101		Mylan Institutional	Not Investigational	
KETAMINE	CN203		JHP Pharmaceuticals	Not Investigational	
PROPOFOL	CN203		APP Pharmaceuticals	Not Investigational	
SEVOFLURANE	CN203		AbbVie Inc.	Not Investigational	
LIDOCAINE HCL	CN204		B Braun	Not Investigational	

2.0 * **Does the local Investigator hold the IND?**

○ Yes ◉ **No**

If yes, please upload the Quality Assessment Summary Report completed by the Research Compliance Officer. NOTE: If the study involves an IND, the Investigator is also required to submit this report to the IDS:

3.0 **Upload the 10-9012 signed by the PI for all investigational drugs used in this research study:**

Modified Date	Name	Description

There are no items to display

4.0 **Upload a Package Insert for all Non-Investigiational (standard of care) Drugs used in this research study:**

Modified Date	Name	Description
12/18/2013 2:40 PM	Remifentanil Insert.pdf	
12/18/2013 2:40 PM	Ketamine Insert.pdf	
12/18/2013 2:40 PM	Propofol Insert.pdf	
12/18/2013 2:41 PM	Sevoflurane Insert.pdf	
12/18/2013 2:41 PM	Lidocaine Insert.pdf	

5.0 **Please upload any Investigator Brochures:**

Modified Date	Name	Description

There are no items to display

ID: Pro00000878 View: 4 Research study methods

Research Study Methods

Describe all study related procedures following enrollment of a subject in this study.

Please see Section 6 for where the study team defines when a subject will be considered enrolled in the study.

1.0

*** Research Procedures/Interventions:**

A total of 48 patients undergoing either inguinal (including femoral) or ventral (including umbilical) herniorrhaphy that requires general anesthesia in the operating room will be enrolled in the study with continuous sampling beginning as soon as the protocol is approved. Inguinal hernias will be the focus, as they are thought to have a higher incidence of chroinc pain; however, ventral herniorraphy may also be used if required to meet study goal numbers. A patient will be considered enrolled in the study when they have passed initial screening questions, signed the consent form, and been randomized to one of three anesthetic technique protocols (TIVA-K, TIVA-R, or BIA). 16 subjects will be used in each group. At the time of first subject enrollment, the subjects will be divided amongst the three groups using a random assignment table generator (www.graphpad.com/quickcalcs/randomize2) stating that A will equal TIVA-K, B will equal TIVA-R, and C will equal BIA. The results will be recorded and followed for all subsequently enrolled patients.

Consistent with our current standard of care, all protocols will begin with perphenazine (up to 8 mg) and acetaminophen (up to 1300 mg) by mouth in the pre-operative holding area, and premedication prior to induction with up to 2 mg of midazolam.

The TIVA-K protocol will consist of the induction of anesthesia with propofol (1-2.5 mg/kg) and ketamine (20 mg), with muscle relaxation being accomplished with either succinylcholine or rocuronium as necessary. Endotracheal intubation may be used for airway management. Anesthesia will be maintained with a propofol infusion (50-150 mcg/kg/min), lidocaine infusion (0.5-1 mg/kg/hr), and ketamine (5 mg each half hour to a maximum of 50 mg). Standard antiemetic medications will be given.

The TIVA-R protocol will consist of the induction of anesthesia with propofol bolus (1-2.5 mg/kg) and the initiation of a remifentanil infusion (0.05-2 mcg/kg/min). Muscle relaxation will be accomplished with either succinylcholine or rocuronium as necessary. Endotracheal intubation may be used for airway management. Anesthesia will be maintained with a propofol infusion (50-150 mcg/kg/min), lidocaine infusion (0.5-1 mg/kg/hr), and continuation of the remifentanil infusion (0.05-2 mcg/kg/min). Standard antiemetic medications will be given.

The BIA protocol will consist of the induction of anesthesia with propofol (1-2.5 mg/kg), with muscle relaxation being accomplished with either succinylcholine or rocuronium as necessary. Endotracheal intubation may be used for airway management. Anesthesia will be maintained with inhaled sevoflurane at a concentration of at least 0.7 MAC and a remifentanil infusion (0.05-2 mcg/kg/min). Standard antiemetic medications will be given.

Surgical modality as dictated by the treating surgeon will be observed and recorded, not randomized. Subcutaneous local anesthetic infiltration will be at the discretion of the surgical team. Post-Anesthesia Care Unit pain medication will consistent of IV hydromorphone and/or PO oxycodone.

Data Collection

Initial data collection will include information on age, gender, height and weight, race, pertinent comorbidities, smoking status, and details about current pain medication use (limited to opioid agonists, tricyclic antidepressants, selective serotonin reuptake inhibitors, and

calcium channel alpha-2-delta ligands [e.g., gabapentin], and non-steroidal anti-inflammatory drugs). This will be collected on the day of surgery, after informed consent has been obtained and the participant has been randomization to anesthetic technique.

The initial data will also consist of baseline measurements of the outcome variables to establish baseline values. These will consist of the study's primary endpoints: the pain numerical rating scale (NRS, the traditional 0-10 pain score where 0 indicts no pain and 10 equates to the most intense pain imaginable), and the revised version of the short form McGill Pain Questionnaire. Additionally, the study's secondary endpoints will be collected: the self-report of the Leeds Assessment of Neuropathic Symptoms & Signs (s-LANSS), and the Pain Quality Assessment Scale (PQAS). The NRS is being used as it will allow us to compare our results with those of historical studies that only used this numerical score. Additionally, in the initial post-operative assessment, it is believed that subjects will not have yet recovered the mental faculties necessary for the more involved scales. The revised short form McGill Pain Score Questionnaire (sf-MPQ-2) is considered by many to be the "gold standard" pain questionnaire, especially for neuropathic pain. The s-LANSS has been shown to discriminate neuropathic from non-neuropathic pain; a score of greater than 12 is considered to be indicative of neuropathic pain (4). Finally, research has shown that the PQAS is able to assess pain changes during and as a result of treatment.

Intra-operative data recorded will include the total amounts of all medications documented on the Anesthesia Record, the surgical approach used (laparoscopic versus open), the type and location of the hernia being repaired, and details on any local anesthetic infusions used by the surgery team.

Follow-up data will be collected at six time points in person or over the phone per convenience including a) post-operative prior to Post Anesthesia Recovery Unit discharge, b) 18-36 hours post-operative, c) 1 months post-operative, d) 3 months post-operative, e) 6 months post-operative, and f) 12 months post-operative. Additional data collected will include details about analgesic use at all time points.

Additionally, intraoperative data will be collected on a subset of 9 of the patients, 3 in each arm. The hypothesis for this study rests on the assumption that the patient’s intraoperative stress response is linked to acute and chronic pain, and that anesthesia technique can affect this stress response. This is supported within the literature through both stress hormone assays[6] and through the analysis of stress-related physical measurements such as heart rate variability[6] and the Surgical Stress Index[9]. This study will collect the variables associated with these physical measurements (continuous electrocardiogram data) to provide pilot data for future study into the link between intraoperative stress and outcome data. To accomplish this, a departmental VA-provided laptop computer will be equipped with an analog-to-digital converter and connected to the analog output of the anesthesia machine. This data will be captured using WINDAQ software (DATAQ Instruments, Inc. Akron, OH) and analyzed off-line with Matlab (Mathworks, Natick, MA). This data does not contain any identifiable data; it is simply voltage level recordings from the OR monitors. The available departmenal VA-laptop computer is compatable with the required software.

Please upload a table of procedures if applicable.
The study procedures table must be completed for:
- All Greater than Minimal Risk (GTM) studies; and
- All Minimal Risk studies that use Standard of Care or Usual Care/Interventions.

Name Modified Date
There are no items to display

2.0 * **Will Usual Care Procedures/Interventions be used?"**

◉ **Yes** ○ No

If yes, please specify and include a description of what the usual care or expected level of care is at VAPHS (e.g., medications, testing, timing, etc.) for patients, similar to those individuals that meet the inclusion/exclusion criteria for this research study:
TIVA with ketamine and/or remifentanil and BIA approaches are considered standard of care for patients undergoing herniorraphy. There are currently no proven advantages for either technique for herniorraphy patients.

2.1 If Usual Care Procedures/Interventions will be used, who is the individual or entity responsible for relevant aspects of the usual care (i.e., which of the above usual care activities will the research study team be responsible for)?:
The Anesthesiologist in charge of the case will ensure that the standard of care is properly followed.

2.2 Does the usual care at VAPHS for the condition of interest in this research study differ from national guidelines/recommendations (i.e. standard of care)?

○ Yes ○ No

If yes, please describe the differences:

2.3 Are any procedures that are considered standard for this patient population performed more frequently than usual care?

○ Yes ○ No

If yes, please indicate which time points are considered usual care and which are considered research.

2.4 If there is more than one standard, does VAPHS limit which one is followed (e.g. warfarin use for atrial fibrillation vs. one of the newer anticoagulants).

○ Yes ○ No

If yes, please explain:

3.0 * **Does clinical expertise need to be enlisted?**

○ Yes ◉ **No**

If yes, please provide the provisions for enlisting the services of a clinician with appropriate expertise and privileges to perform duties, if the investigator is not a clinician [i.e. reviewing the data, adverse events, and new study findings; also making required decisions to protect the health of the subject (e.g., stopping the participant's involvement in the study or determining when to notify the subject or the subject's health care provider of information that may affect the health of the subject)]:

4.0 **Please upload any surveys, questionnaires, and data collection forms.**

	Document	Description	Version Number
View	StudyDataFormFull.pdf(0.01)		0.01

ID: Pro00000878 View: 4.1 Research study methods: analysis Plan

1.0 * **Please describe the analysis plan for the study** *(it is acceptable to refer to the sponsor/multi-site protocol for section if applicable):*

The primary outcome is the overall incidence of CNP and will be compared across the three arms: TIVA-R, TIVA-K, and BIA protocol. This is a pilot study, as direct numbers for the estimation of the sample size are not available, given the varied incidence of chronic pain (10 to 63%) found in the literature, and the fact that anesthetic technique is typically not presented with this data. Because our hypothesis is that technique will affect CNP though the anesthetic technique's effect on the surgical stress response, we reviewed the literature surrounding this phenomenon. Significant differences in the circulating catecholamine concentration and in heart rate variability patterns has been observed in a study comparing BIA to TIVA (without specifying if ketamine or remifentanil were used) with 43 patients(6). The link between intraoperative stress and acute (24 hour postoperative) pain was demonstrated in a study of 34 subjects(11) using heart rate variability as a measure of stress, and in a study of 45 subjects using serum catecholamines(8). While this provides little guidance for technique's effect on chronic pain, it provides a starting point for pilot work. Therefore, we are targeting 48 patients, 16 in each group. Subject recruitment numbers will be closely monitored, and the randomization technique may be modified as the study nears completion to ensure balanced groups.

The surgical details and demographic data for each patient will be recorded on the data collection forms. This information will then be de-identified and entered into SPSS (v.21, SPSS, Inc., Chicago, Il.). SPSS is a program that performs statistical calculations. It resembles Microsoft Excel in terms of layout but is able to handle the advanced calculations required for statistical analysis.

Categorical data (demographics) will be tested with a Fisher's exact test (for 2x2 tables) or a Chi-square, both with two-sided tails. Continuous variables will be compared with a two-sample t-test. An overall p-value of 0.05 with Bonferroni or other relevant correction for multiple comparisons will be used for significance. If any of these vary significantly between the groups, multivariate techniques will be used instead of the univariate approach described below.

All outcome variables (NRS, s-LANSS, PQAS, sf-MPQ) are ordinal data, and as such will require non-parametric testing. As the study is progressing, the techniques will be compared via Kruskal-Wallis testing at each time interval. The presence of CNP will be defined as a positive S-LANSS (scores ≥ 12 are highly suggestive of neuropathic pain); after the 3 month time point will be considered "chronic". These definitions are consistent with the literature and with published standards.(2,4) Thus, for the 6 and 12 month time points, the incidence of CNP for each technique will be computed and compared via chi-squared analysis.

Interim analyses are planned for 3, 6, 9 and 12 months, with the major focus being a definitive power analysis for variables found to be non-significant (as this is a pilot study). Because this study involves no changes to standard of care for herniorrhaphy surgery patients, stopping the study prematurely based on these interim analyses is not expected.

As planned, a continuous sampling of patients undergoing umbilical or inguinal herniorrhaphy will be included in this study. In addition, all equipment and personal required for this study are already in place within the VAPHS. Therefore, time for patient enrollment or equipment procurement is not necessary, and this study can begin as soon as all approvals (including IRB, R&D and ACOS) are granted. The study will continue for at least 1 year. The decision to continue past this time will be based on the achieved statistical power after 12 months of data collection. Because the data will be entered throughout the year and analyzed at 3 month

intervals, the time required for final analysis will be minimal. Submission for publication is expected within 3 to 12 months of the completion of data collection.

ID: Pro00000878 View: 5 Sub-Studies

1.0 * **Is there a sub-study or are there sub-studies associated with this study?**
There is no sub-study associated with this study.

ID: Pro00000878 View: 6 Study Population Summary

Study Population Summary

1.0 * **What is the maximum number of subjects you plan to enroll at VAPHS?**
60

2.0 * **Do you plan on enrolling patients into different categories:**
○ Yes ◉ **No**

If yes, please explain:

3.0 **If this is a multi-site study, indicate the projected total subject accrual:**

4.0 * **Please provide a justification for the sample size:**
As copied from the analysis plan, the primary outcome is the overall incidence of CNP and will be compared across the three arms: TIVA-R, TIVA-K, and BIA protocol. This is a pilot study, as direct numbers for the estimation of the sample size are not available, given the varied incidence of chronic pain (10 to 63%) found in the literature, and the fact that anesthetic technique is typically not presented with this data. Because our hypothesis is that technique will affect CNP though the anesthetic technique's effect on the surgical stress response, we reviewed the literature surrounding this phenomenon. Significant differences in the circulating catecholamine concentration and in heart rate variability patterns has been observed in a study comparing BAL to TIVA (without specifying if ketamin or remifentanil were used) with 43 patients(6). The link between intraoperative stress and acute (24 hour postoperative) pain was demonstrated in a study of 34 subjects(11) using heart rate variability as a measure of stress, and in a study of 45 subjects using serum catecholamines(8). While this provides little guidance for technique's effect on chronic pain, it provides a starting point for pilot work. Therefore, we are targeting 48 patients, 16 in each group. Subject recruitment numbers will be closely monitored, and the randomization technique may be modified as the study nears completion to ensure balanced groups.

ID: Pro00000878 View: 6.1 Study Population

Study Population

1.0 * **Check all that apply to describe your study population:**

Study Population
☐ Non-Veterans
☐ Special Populations
☑ **Veterans**
☐ Vulnerable populations
☐ Other

2.0 * **Indicate the inclusion criteria for enrollment:**
All of the patients undergoing herniorrhaphy surgery that requires general anesthesia at VAPHS will be eligible for the study. Subjects will not be specifically excluded based on their race, religion, ethnicity, gender or HIV status.

3.0 * **Indicate exclusion criteria for enrollment:**
Subjects will be excluded who are unable to communicate directly with the investigators, due to being non-English speaking, loss of hearing, or incompetence. Subjects with any of the following will also be excluded including a history of malignant hyperthermia, pseudocholinesterase deficiency, or other disease that prevents anesthetic randomization; pain-related disorders such as fibromyalgia or other chronic pain syndromes; or emergency surgery.

4.0 **If there are any age, ethnic, language, or gender-based exclusion criteria, including the exclusion of any pregnant or lactating women, or those of child-bearing potential, please provide justification:**
This study is based on patient-reported data using pain surveys that have not been validated across multiple languages, therefore potential subjects must be able to communicate directly in English. Pregnancy would be clinically evaluated as a standard of care by the Anesthesia Department prior to exposure to anesthesia and as such would not be a research activity. Furthermore, any woman who tests positive for pregnancy will be excluded from the study.

5.0 **Please specify why vulnerable subjects and/or special populations will not be enrolled:**

6.0 **With some exceptions as listed in VHA Handbook 1200.05, incompetent subjects cannot be enrolled in VAPHS approved research. Specify that you will not enroll incompetent subjects and the general rules to be used in making that determination:**
Due to the necessity of patient-reported data throughout the study, incompetent subjects for whom consent for surgery and anesthesia has to be obtained from next of kin/power of attorney will be excluded from the study.

ID: Pro00000878 View: 7 Risk/Benefit Assessment-Risks

Risk/Benefit Assessment-Risks

1.0 * **Risk classification for this study (select one).**

Name
○ Minimal Risk
◉ **Greater than Minimal Risk**

2.0 * **Basis for making the above recommendation:**

This study will pose greater than minimal risk to the subjects. All anesthetic techniques are within the standards of best practice for patients undergoing herniorrhaphy with general anesthesia, however the study involves randomization into one of two anesthetic approaches with potential side effects. The individual may experience side effects that he would not have experienced if a different regimen was chosen. The proposed intervention will not alter surgical modality as previously determined by the treating physician.

Other risks include the very rare risk for a breach of confidentiality. The precautions detailed below will be used to minimize this risk.

3.0 * **Describe the safety precautions that will be taken to minimize risks/harms:**

The only paper form that will contain patient-identifiable data will be the list of enrolled patients and their corresponding study subject number. This will be stored in a locked cabinet in a locked office accessible only to the primary investigator or other designated physcian co-investigator. Patient study forms will consist of the data collected throughout the study period beginning with preoperative assessment. No patient-identifiable information is included on this form (see form attached). These forms will be filed in a separate locked filing cabinet. Only the PI and co-investigators will have access to this information. All de-identified data gathered from the pain report forms and entered into the analysis program will be stored in a password-protected location on the VAPHS network.

4.0 * **Provide details regarding the nature of each risk using the area provided below:**

	Risk Name
View	Remifentanyl administration
View	Ketamine administration
View	Patient Survey
View	Sevoflurane
View	Propofol adminstration

5.0 * **Do you plan on using the research answering service:** ◉ **Yes** ○ No

If yes, please Upload the research answering service form:
Research_Answering_Service_Ibinson.doc(0.01)

6.0 **If your study involves a treatment or intervention, please upload the Patient ID Card:**

ID: Pro00000878 View: 7.1 Risk/Benefit Analysis-Potential Benefits and Alternatives

Risk/Benefit Analysis-Potential Benefits and Alternatives

Describe any potential for benefits to participants in this study:

1.0 * **Direct and Indirect Benefits to Subjects:**
Subjects will not receive any direct benefit from this study. As this is pilot work, this study's chief benefit is that of generalizable knowledge, in that the data gathered within will provide a foundation for a larger study designed to probe the association of each main medication in the TIVA and BAL protocols with acute and chronic pain. The only potential for subject benefit would be if the hypothesis that a TIVA-based approach will lead to less chronic pain was proven to be true, and thus subjects randomized to the TIVA group would be less likely to develop chronic pain.

2.0 * **Describe alternatives (research or non-research) that are available to subjects if they choose not to participate in this study:**
If subject choose to not participate in the study, they can receive surgery with the anesthesia as chosen by the anesthesiologist assigned to the case.

ID: Pro00000878 View: 8 Methods of Recruitment and Retention

Recruitment Methods and Materials used for Retention

1.0 * **Select recruitment methods used on this study:**

Name	
☐	Mail Campaign
☐	Referral by independent source
☐	Advertising such as fliers, letters, or ads (newspaper, TV, radio)
☐	Web Site
☐	Research registry
☐	Selected from pre-existing records
☐	Pre-existing relationship with participants
☑	**Other**

If Other Methods Specify:
Subjects will be recruited based on their referral to the Interdisciplinary Medical Perioperative Assessment Consultation Treatment (IMPACT) clinic, as described below.

2.0 * **Specify how subjects will be identified and how study eligibility will be determined:**
A total of 48 (16 in each of three groups) patients undergoing either inguinal (including femoral) or ventral (including umbilical) herniorrhaphy that requires general anesthesia in the operating room will be enrolled in the study with continuous sampling. A patient will be considered enrolled in the study when they have passed initial screening questions, signed the consent form, and been randomized. Subject recruitment will occur through In-person or e-consult paths, both described below.

IMPACT In-person Visit
General surgery patients are referred to the Interdisciplinary Medical Perioperative Assessment Consultation Treatment (IMPACT) clinic for routine medical and functional evaluations prior to surgery. These include patient history, physical examination, and other evaluations in routine patient care that do not typically include the detailed pain status questionnaires to be used in this study. During the in-person consult, Dr. Visala Muluk reviews each patient's medical record, determining if the patient is medically optimized and ready for their scheduled surgery. At this time, Dr. Muluk will also screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. If so, she will briefly describe the study as follows:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, you would recieve a standard anesthetic combination, but it would be randomly chosen from several standard approved combinations now available. They would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). Do you think you might be interested in participating? [If "no", STOP] [If "yes", CONTINUE]

With your permission, I would like to share the details of your upcoming surgery and the history I collected with them so that they can discuss this study with you to see if you are interested. To do so, I need your consent to share this information."

Dr. Muluk will then ask for the patient's approval to share the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with Dr. Ibinson (study PI). If the patient agrees, Dr. Muluk will also provide the potential subject with a copy of the Informed Consent form for their review. Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

Dr. Ibinson will then be notified of the patient's possible interest via phone call or secure, encrypted VA email. Dr. Ibinson will contact (in person if possible; if not, via telephone) the patient to explain the procedures of the study using the attached script if they are eligible. All patient questions will be answered, and the patient will be told that all signatures will be obtained on the informed consent document on the day of surgery after any additional questions are answered.

When the patient presents on the day of surgery, Dr. Ibinson will review the patient's information, inquire about any health status or operative plan changes, and obtain informed consent. The patient's name will be added to the master list of subjects once they consent to screening. The master list of subjects will be stored electronically on the VAPHS network, and this list will only be viewable to the PI. The patient will then be randomized to one of three anesthetic technique protocols (TIVA-K, TIVA-R, or BIA) using a computer-generated random numbers table. Following this, the baseline information (including the demographics and pain survey scores included on the research study forms) will be collected.

IMPACT e-Consult
Instead of in-person consult for general surgery patients, e-consults are sometimes performed by the IMPACT team via phone for routine medical and functional evaluations prior to surgery. These include examining the electronic medical record for patient history and other evaluations in routine patient care that do not typically include the detailed pain status questionnaires to be used in this study. During the e-consults for hernia repair surgery, the IMPACT staff member will briefly state the following:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, they would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). If you are interested in participating in this study, please contact Dr. Visala Muluk at 412-688-6113 for more details."

The IMPACT staff member will not screen for study eligibility; all patients for hernia repair will be given this information. Patient contact with Dr. Muluk is being requested due to her availability via telephone during business hours. If the patients are interested and contact Dr. Muluk, she will screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. If so, she will briefly describe the study as follows:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, you would receive a standard anesthetic combination, but it would be randomly chosen from several standard approved combinations now available. They would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). Do you think you might be interested in participating? [If "no", STOP] [If "yes", CONTINUE]

With your permission, I would like to share the details of your upcoming surgery and the history that I collected with them so that they can discuss this study with you to see if you are interested. To do so, I need your consent to share this information. They will also mail a copy of the consent form to you so that they can go over it with you."

Dr. Muluk will then obtain verbal HIPAA consent prior to sharing the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with Dr. Ibinson (study PI). Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

Dr. Ibinson will then be notified of the patient's possible interest via phone call or secure, encrypted VA email. Dr. Ibinson will contact (via telephone) the patient to explain the procedures of the study using the attached script if they are eligible. All telephone contacts will begin by referring to the subject's (possible) participation in the research study. All patient questions will be answered. The patient will be told that while all signatures will be obtained on the informed consent document on the day of surgery after any additional questions are answered.

When the patient presents on the day of surgery, Dr. Ibinson will review the patient's information, inquire about any health status or operative plan changes, and obtain informed consent. The patient's name will be added to the master list of subjects once they consent to screening. The master list of subjects will be stored electronically on the VAPHS network, and this list will only be viewable to the PI. The patient will then be randomized to one of three anesthetic technique protocols (TIVA-K, TIVA-R, or BIA) using a computer-generated random numbers table. Following this, the baseline information (including the demographics and pain survey scores included on the research study forms) will be collected.

3.0 * **Provide the location (or locations) of the sites where participants will be recruited:**
For the in-person visit path, recruitment will begin in the IMPACT clinic, continuing when the patient talks with Dr. Ibinson either in-person or over the telephone. There will be a check for any pertinent changes that may have occurred in each patient's health information and surgical plan being performed in the Same-Day Surgery holding area on the day of surgery prior to the informed consent document being signed.

For the e-consult path, recruitment will occur via phone, with an informed consent being signed (and a check for any pertinent changes that may have occurred in each patient's health information and surgical plan being performed) in the Same-Day Surgery holding area on the day of surgery.

4.0 **Please include information regarding any advertisements (print, TV, radio, etc) that will be used to recruit subjects including a general description of where this information will be posted:**
None.

5.0 **Please UPLOAD the documents that will be used for recruitment and an introductory statement or letter to accompany consent for those studies obtaining written informed consent using methods such as fax, email or mail (if applicable). Please also upload any screening/recruitment questions that will be verbally asked of potential research subjects. Also, if you will be providing any retention materials, please upload them here.**

Name	Reviewer	Modified Date	Version Number
There are no items to display			

ID: Pro00000878 View: 9 Informed Consent

Informed Consent

1.0

*** Indicate the types of consent that will be involved in this study (check any or all that apply):**

Informed Consent Category
Written/signed consent by subject
Waivers are being requested.
Verbal consent or written information sheet(Requires a Waiver of Documentation of Informed Consent - see below)

2.0 *** Waivers: If you are applying for any waivers of consent (check any or all that apply):**

Name	
☑	**Waiver of Informed Consent**
☑	**Waiver of HIPAA Authorization**
☑	**Waiver of Documentation of Informed Consent (telephone consent, verbal script)**
☐	No Waiver at all

3.0 *** Will this study include non-English speaking participants?**

○ Yes ◉ **No**

ID: Pro00000878 View: 9.1 Waiver of HIPAA

You have indicated you are requesting a waiver of HIPAA.

1.0 * **Is the request only for Screening/Recruitment purposes?**

◉ **Yes** ○ No

If yes, please describe your screening/recruitment method:
As described in Section 8: General surgery patients are referred to the Interdisciplinary Medical Perioperative Assessment Consultation Treatment (IMPACT) clinic for routine medical and functional evaluations prior to surgery. These include patient history, physical examination, and other evaluations in routine patient care that do not typically include the detailed pain status questionnaires to be used in this study. During the in-person consult, Dr. Visala Muluk reviews each patient's medical record, determining if the patient is medically optimized and ready for their scheduled surgery. At this time, Dr. Muluk will also screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. If so, she will briefly describe the study, and ask for the patient's approval to share the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with Dr. Ibinson (study PI). Dr Ibinson will ask screening questions regarding prior anesthesia and chronic pain. Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

Occasionally, e-Consults are used for patient pre-operative evaluation by the IMPACT staff. In this case, the IMPACT staff member will briefly state the following:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, they would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). If you are interested in participating in this study, please contact Dr. Visala Muluk at 412-688-6113 for more details."

The IMPACT staff member will not screen for study eligibility; all patients for hernia repair will be given this information. Patient contact with Dr. Muluk is being requested due to her availability via telephone during business hours. If the patients are interested and contact Dr. Muluk, she will screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. Dr. Muluk will then inform the patient of their eligibility and if eligible, obtain verbal HIPAA consent prior to sharing the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with the Dr. Ibinson (study PI). Dr Ibinson will ask screening questions regarding prior anesthesia and chronic pain. Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

If no, the request is for the full study (e.g. retrospective chart reviews and certain observational studies)

Please describe the types of records and/or databases to be accessed:

THE IDENTIFIABLE INFORMATION BEING REQUESTED:
Note: If participants will be receiving payment and HIPAA Authorization is not being obtained, you must select Names, Addresses and Social Security Numbers as that information will be disclosed for payment purposes.

2.0 * **Identifiable Information per HIPAA Definition**

	Name
☐	None
☐	Account numbers
☐	Biometric identifiers, including finger and voice prints
☐	Certificate/license numbers
☐	Device identifiers and serial numbers
☑	**Elements of dates (except year, for example, date of birth, admission date, discharge date, date of death, date of procedures; and all ages over 89)**
☐	Email Address
☐	Fax Numbers
☐	Full-face photographic images or any comparable images
☐	Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)
☐	Health plan beneficiary numbers
☐	Internet Protocol (IP) address numbers
☐	Medical Record Numbers
☑	**Name or any derivative of name such as initials**
☑	**Social Security Numbers**
☑	**Telephone Numbers**
☐	URLs (Web Universal Resource Locators)
☐	Vehicle identifiers and serial numbers, including license plate numbers
☐	Any other unique identifying number, characteristic, or code (Note: The study ID number, code or other means of record identification is not considered one of the identifiers that must be excluded for de-identification)

3.0 * **Patient Protected Health Information:**

	Name
☑	**Demographic Information (e.g., Name, Address, Phone Number, Social Security Number**
☐	Billing and Payment Information
☑	**Hospital or Medical Records**
☑	**History and Physical Exam Notes**
☐	Mental Health Records
☐	Data Previously Collected for Research Purposes
☑	**Progress Notes**
☐	Consultation Reports
☐	Laboratory Test Results
☐	Operative Reports
☐	Other

Please indicate the 'Other' Patient Protected Health Information:

4.0 **Other Health Information:**

Name
There are no items to display

ID: Pro00000878 View: 9.1.1 Waiver of HIPAA - More Information

Waiver of HIPAA- More Information

1.0 * **Describe how the identifiable information is to be used and/or disclosed only by members of the research team and the following persons *(identify with specificity and justify the need to disclose the information to anyone outside the VHA.)* Note: If participants will be receiving payment and HIPAA Authorization is not being obtained, you must also describe this disclosure to representatives of the VA for administrative purposes here.**

Also describe how this activity meets the "minimum necessary standard" described in the HIPAA Privacy Rule:
The waiver is:

A. For Dr. Muluk to prescreen the medical records for potential eligibility (inclusion/exclusion criteria).

B. To pass along information (i.e., patient's name and contact information, scheduled surgery, and IMPACT Pre-operative evaluation) to the PI of individuals who agree to be contacted.

This procedure meets the "minimum necessary standard' as described in the HIPAA Privacy rule due to the fact that Dr. Muluk would be reviewing the medical record for the information for clinical reasons and the PI will only receive the information necessary to contact eligible and interested patients.

The proposed study poses minimal risk to the privacy of the subjects because...

2.0 * **Describe how the identifiable information will be protected from improper use or disclosure by (detail how this will be accomplished including the limitations of physical or electronic access to the information and other protections):**
If the patient agrees to further contact with the research team, the Dr. Muluk will then notify Dr. Ibinson via in-person communication or through secure, encrypted VA email.

3.0 * **Describe how the identifiers will be destroyed at the earliest opportunity consistent with the research (discuss the timeframe or the reasons the identifiers must be retained, including health or research justifications or any legal requirement to retain them) (Note: At this time, identifiers used for research screening and all other screening records must be retained indefinitely and this must be documented by checking "Other" below):**
After contacting the potential subject, the PI will delete the email from his account. If the subject agrees to participate after receiving the complete study information, then the patient's name will then be added to the master list of subjects. The master list of subjects will be stored electronically on the VAPHS network, as described elsewere, and this list will only be viewable to the PI.

All research records will be maintained in accordance with the Veterans Health Administration (VHA) Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS Privacy Officer, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.

* **When will screening data be de-identified or destroyed:**
Name

subject contact (e.g. mailings)
If Other, please describe:

4.0 * **Describe how the identifiable information will not be reused or disclosed to any other person or entity outside the VHA other than the manner described in the protocol, except as a required by law, for authorized oversight of this research study, or as specifically approved for used in another study by an IRB:**
Participant information will not be reused or disclosed to any other person or entity outside of the VHA. Participant information may be disclosed to the VAPHS Research and Development Office Staff in order for them to perform duties related to research administration. Additionally,

participant information may be shared with the VAPHS IRB in order to ensure the protection of human subjects, staff of the VAPHS Research Compliance Office in order to perform audit and compliance duties, and federal agencies, such as the VA Office of Research Oversight (ORO), the Office for Human Research Protections (OHRP) and the Government Accounting Office (GAO), in order to meet VA and other federal or local regulations. Research records may be released or disclosed pursuant to applicable federal and state law, as well as to federal and state agencies that are responsible for medical research oversight. Additionally, any medical information may be shared with the participant's healthcare provider(s) with his or her consent, and possibly without his or her consent if permissible under federal laws and regulations.

5.0 * **Describe why the proposed study cannot be practicably conducted without a waiver of authorization: (discuss reasons why it would not be possible to obtain authorization from individual subjects. Time constraints themselves are generally not considered adequate for this justification:**

The recruiting methods of this study would become nearly impossible without this waiver of authorization for screening purposes due to the fact that the contact with study staff will occur during and after a telephone-based e-consult.

6.0 * **Describe why the proposed study cannot be done without the specified identifiable information: Discuss reasons why it would not be possible to conduct the research without the identifiable information being collected.**

Without the patient's contact information, the research team will not be able to contact those patients interested in participating in the study.

ID: Pro00000878 View: 9.2 Waiver of Informed Consent

Waiver of Informed Consent

1.0 * **The proposed study poses minimal risk to the subjects because (outline the subject's involvement in the project and why the study poses minimal risk):**

This study will pose minimal risk to the subjects since all anesthetic techniques are within the standards of best practice for patients undergoing herniorrhaphy with general anesthesia. The proposed intervention will not alter surgical modality as previously determined by the treating physician. The backbone of the study is the collection of the data via the survey instruments, which carries only the very rare risk for a breach of confidentiality. The precautions detailed in the risk section will be used to minimize this risk.

2.0 * **The waiver will not adversely affect the rights and welfare of the subjects because:**

The waiver is being requested to allow Dr. Muluk to review the records for the inclusion/exclusion of the study and to share information on interested subjects, including the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with Dr. Ibinson. The Pre-operative evaluation is information that Dr. Muluk would have as part of her clinical duties and Dr. Ibinson would have access to in any case, if he was assigned to care for the patient on the day of surgery.

3.0 * **The research could not reasonably be carried out without the waiver because:**

I significant portion of patients scheduled for the repair of hernias are able to complete their pre-operative evaluation via the e-consult route. It would be impractical to ask patients to come to IMPACT clinic for the sole purpose of signing the waiver.

4.0 * **The research could not practicably be carried out without using identifiable private information or identifiable biospecimens because:**

5.0 * **When appropriate, subjects will be provided with the following additional pertinent information after participation (if you have no plans to provide additional information to subjects please provide justification):**

This waiver is only being requested for screening and recruitment purposes. Patient involvement will be considered complete after the final questionnaires are administered 12 months after surgery. The results of the study will then be compiled, analyzed, described, and published. While any practical effect the type of anesthesia each individual patient received would have little impact on the patient's future medical history, the study's published results will be available electronically.

ID: Pro00000878 View: 9.3 Waiver of Documentation of Informed Consent

Waiver of Documentation of Informed Consent

You have selected a waiver of Documentation of Informed Consent

1.0 **This is a request for Waiver of Documentation of Informed Consent because this research study conforms to either A and/or B (Check if 'yes' and provide the verifying information requested):**

* A: The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern. ○ Yes ◉ **No**

AND/OR

* B: The proposed study poses minimal risk to the subjects. ◉ **Yes** ○ No

If yes, please explain why the proposed study poses minimal risks to the subjects. (Outline the subject's involvement in the project and why the study poses minimal risk) :
This study will pose minimal risk to the subjects since all anesthetic techniques are within the standards of best practice for patients undergoing herniorrhaphy with general anesthesia. The proposed intervention will not alter surgical modality as previously determined by the treating physician. The backbone of the study is the collection of the data via the survey instruments, which carries only the very rare risk for a breach of confidentiality. The precautions detailed in the risk section will be used to minimize this risk.

2.0 * **The research involves no procedures for which written consent is normally required outside of the research context. Research procedures include:**
For this waiver, the procedures only include the sharing of information of interested patients with the PI so that he can contact the potential subject and further describe the study. All subjects that participate in the full study will reivew and sign an informed consent document.

3.0 * **Explain how whenever appropriate, the subjects will be provided with additional pertinent information (e.g. an information sheet):**
This waiver is only being requested for screening and recruitment purposes. Patient involvement will be considered complete after the final questionnaires are administered 12 months after surgery. The results of the study will then be compiled, analyzed, described, and published. While any practical effect the type of anesthesia each individual patient received would have little impact on the patient's future medical history, the study's published results will be available electronically.

4.0 **Please upload SCRIPT here:**

	Document	Description	Version Number
View	Ibinson Study Description Script v4.doc(0.04)		0.04

ID: Pro00000878 View: 9.4 Consent Forms & Process of Consent

Consent Forms & Process of Consent

1.0 Upload the completed forms into the correct lists below.

1.1 **Informed Consent Form (clean copy):**

	Document	Modified Date	Version Number
View	Consent 2017 PRO878 Clean v12(0.01)	5/5/2017 12:00 AM	0.01

1.2 **Provider Behavior Informed Consent Form (clean copy):**

Document	Modified Date	Version Number
There are no items to display		

1.3 **Screening Informed Consent Form (clean copy):**

Document	Modified Date	Version Number
There are no items to display		

2.0 **Consent Forms (modified copy):**

	Document	Modified Date	Version Number
View	Consent_2017_Tracked Changes.docx(0.01)	5/4/2017 2:27 PM	0.01

3.0 * **Describe how, where, when, and by whom the consent process will be initiated:**

A total of 48 (16 in each of three groups) patients undergoing either inguinal (including femoral) or ventral (including umbilical) herniorrhaphy that requires general anesthesia in the operating room will be enrolled in the study with continuous sampling. A patient will be considered enrolled in the study when they have passed initial screening questions, signed the consent form, and been randomized. Subject recruitment will occur through In-person or e-consult paths, both described below.

IMPACT In-person Visit
General surgery patients are referred to the Interdisciplinary Medical Perioperative Assessment Consultation Treatment (IMPACT) clinic for routine medical and functional evaluations prior to surgery. These include patient history, physical examination, and other evaluations in routine patient care that do not typically include the detailed pain status questionnaires to be used in this study. During the in-person consult, Dr. Visala Muluk reviews each patient's medical record, determining if the patient is medically optimized and ready for their scheduled surgery. At this time, Dr. Muluk will also screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. If so, she will briefly describe the study as follows:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, you would recieve a standard anesthetic combination, but it would be randomly chosen from several standard approved combinations now available. They would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). Do you think you might be interested in participating? [If "no", STOP] [If "yes", CONTINUE]

With your permission, I would like to share the details of your upcoming surgery and the history I collected with them so that they can discuss this study with you to see if you are interested. To do so, I need your consent to share this information."

Dr. Muluk will then ask for the patient's approval to share the patient's name, scheduled surgery, and IMPACT Pre-operative evaluation with Dr. Ibinson (study PI). If the patient agrees, Dr. Muluk will also provide the potential subject with a copy of the Informed Consent form for their review. Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

Dr. Ibinson will then be notified of the patient's possible interest via phone call or secure, encrypted VA email. Dr. Ibinson will contact (in person if possible; if not, via telephone) the patient to explain the procedures of the study using the attached script if they are eligible. All patient questions will be answered, and the patient will be told that all signatures will be obtained on the informed consent document on the day of surgery after any additional questions are answered.

When the patient presents on the day of surgery, Dr. Ibinson will review the patient's information, inquire about any health status or operative plan changes, and obtain informed consent. The patient's name will be added to the master list of subjects once they consent to screening. The master list of subjects will be stored electronically on the VAPHS network, and this list will only be viewable to the PI. The patient will then be randomized to one of three anesthetic technique protocols (TIVA-K, TIVA-R, or BIA) using a computer-generated random numbers table. Following this, the baseline information (including the demographics and pain survey scores included on the research study forms) will be collected.

IMPACT e-Consult
Instead of in-person consult for general surgery patients, e-consults are sometimes performed by the IMPACT team via phone for routine medical and functional evaluations prior to surgery. These include examining the electronic medical record for patient history and other evaluations in routine patient care that do not typically include the detailed pain status questionnaires to be used in this study. During the e-consults for hernia repair surgery, the IMPACT staff member will briefly state the following:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, they would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). If you are interested in participating in this study, please contact Dr. Visala Muluk at 412-688-6113 for more details."

The IMPACT staff member will not screen for study eligibility; all patients for hernia repair will be given this information. Patient contact with Dr. Muluk is being requested due to her availability via telephone during business hours. If the patients are interested and contact Dr. Muluk, she will screen the patient's medical record to determine if the patient meets the study's inclusion and exclusion criteria and could be a potential candidate. If so, she will briefly describe the study as follows:

"Several of the physicians of our anesthesia department are interested in understanding how the amount of pain you feel after a surgery to repair a hernia can be influenced by the type of anesthesia medications you receive during your surgery. For this study, you would receive a standard anesthetic combination, but it would be randomly chosen from several standard approved combinations now available. They would like to ask you questions about your pain both before and after your surgery (which they can do over the phone). Do you think you might be interested in participating? [If "no", STOP] [If "yes", CONTINUE]

With your permission, I would like to share the details of your upcoming surgery and the history that I collected with them so that they can discuss this study with you to see if you are interested. To do so, I need your consent to share this information. They will also mail a copy of the consent form to you so that they can go over it with you."

Waivers of HIPAA, informed consent, and documentation of informed consent have been requested for the screening and sharing of information described above.

Dr. Ibinson will then be notified of the patient's possible interest via phone call or secure, encrypted VA email. Dr. Ibinson will mail a copy of the informed consent form to the patient and then contact (via telephone) the patient to explain the procedures of the study using the attached script if they are eligible. All telephone contacts will begin by referring to the subject's (possible) participation in the research study. All patient questions will be answered. The patient will be told that while all signatures will be obtained on the informed consent document on the day of surgery after any additional questions are answered.

When the patient presents on the day of surgery, Dr. Ibinson will review the patient's information, inquire about any health status or operative plan changes, and obtain informed consent. The patient's name will be added to the master list of subjects once they consent to screening. The master list of subjects will be stored electronically on the VAPHS network, and this list will only be viewable to the PI. The patient will then be randomized to one of three anesthetic technique protocols (TIVA-K, TIVA-R, or BIA) using a computer-generated random numbers table. Following this, the baseline information (including the demographics and pain survey scores included on the research study forms) will be collected.

4.0 * **Will you be maintaining a Master List of Subjects?**
Yes

5.0 * **Describe when the subject's name will be added to the master list and how the list will be maintained in a secure fashion.**
The patient's name will be added to the master list of subjects at screening. The master list of subjects will be stored electronically on the VAPHS network, and this list will only be viewable to the PI.

ID: Pro00000878 View: 10.0.0 Data Security and Privacy: Data Types Storing

10.0 Data Types Collecting and Storing

1.0 **Click the add button (below) to open an entry form to indicate the types and/or sources of the data that will be collected/stored as part of the project.**

Instructions: **For each type/source of data that will be collected as part of the project, this includes screening data, click the add button to open an entry form that lists the types and/or sources of data. Select a source/type of the data that will be collected/stored. Then indicate what, if any, identifiers or sensitive information will be collected/stored from the source/type (None is an option). To add another source/type click "OK Add Another" button to open up a new entry form to repeat the process.**

Example 1: You are collecting data from VA Medical records including names, last 4 of SSN, and addresses. Therefore, you would select "VA medical record data" as the source, and then select in the identifiers: "Name or any derivative of name, such as initials," "Social Security Numbers," and "Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)" as the identifiers being collected.

Example 2: You are screening VA Medical Records and recording the information you use to screen (i.e.: names, last 4 of SSN, and addresses, etc.) Note: This information must be treated as a Source document, please select "Screening" as the source and then select the identifiers "Name or any derivative of name, such as initials," "Social Security Numbers,", as applicable.

*

	Data Type/Source	Collection Details	Identifiers
View	Questionnaires/Surveys, paper	Patient study forms will consist of the data collected throughout the study period beginning with preoperative assessment. No patient-identifiable information is included on this form. Only the PI and co-investigators will have access to this information. All de-identified data gathered from the pain report forms and entered into the analysis program will be stored in a password-protected location on the VAPHS network. All paper records will be stored in a locked office and inside a locked cabinet accessible only to the primary investigator.	None
View	VA medical record data (i.e., diagnoses, procedures, visits) via **chart review**	The only form that will contain patient-identifiable data will be the master list of enrolled patients (collected and recorded by the PI) and their corresponding study	Elements of dates (except year, for example, date of birth, admission date, discharge

Data Type/Source	Collection Details	Identifiers
	subject number. This will be stored electronically under the PI's account on the VAs password protected network.	date, date of death, date of procedures; and all ages over 89)
		Medical Record Numbers
		Telephone Numbers
		Social Security Numbers
		Geographical subdivisions smaller than a State (street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code)
		Name or any derivative of name such as initials

ID: Pro00000878 View: 10.0.1 Data Security and Privacy: Social Security Numbers

10.0.1 Data Security and Privacy: Social Security Numbers

1.0 You indicated that you will be using all or some part of the research subjects' SSNs as part of this study. Which of the following will you be using:

Real Social Security numbers	*	(●) **Yes** ( ) No
Scrambled Social Security numbers	*	( ) Yes (●) **No**
Last 4 digits of Social Security Number	*	( ) Yes (●) **No**
Other (some derivation of the SSN)	*	( ) Yes (●) **No**

If other, please explain:

2.0 * Please describe how subjects' Social Security numbers will be used in this study:
Social security numbers (as the medical record numbers) will be maintained on the master list of subjects so that each subject can be contacted by the PI for the 1 through 12 month surveys of pain as the study progresses.

3.0 * Please describe the security measures that will be taken to protect SSNs.
The SSN's will only be recorded on the master subject list; therefore, as described for the master list, will be stored on the primary investigators secure, password protected VA computer account.

ID: Pro00000878 View: 10.1.0 Data Security and Privacy: Incoming Data

10.1.0 Incoming Data

1.0 * **Will data be transferred into VAPHS?**

No. Data is not being transferred into this facility

ID: Pro00000878 View: 10.2.0 Data Security and Privacy: Outgoing Data

10.2.0 Outgoing Data

1.0 * **Will any of the data being collected/stored be transferred outside of VAPHS?**

No. The data is not being transferred outside of this facility.

ID: Pro00000878 View: 10.3.0 Data Security and Privacy: Local Data Storage Types

10.3.0 Local Data Storage Types

1.0 * **How will data be stored on this project? (Select all that apply)**

On Paper

Electronically

ID: Pro00000878 View: 10.3.1 Data Security and Privacy: Local Data Storage Types - Paper

10.3.1 Local Data Storage Types - Paper

1.0 * **All VA research data collected in paper must be stored in a locked room at VAPHS. List the room number(s) and the campus(es) where data will be stored in the text box below.**

VA Pittsburgh Healthcare System
Anesthesia Service Rm 3N221N
University Drive C
Pittsburgh, PA 15240

ID: Pro00000878 View: 10.3.2 Data Security and Privacy: Local Data Storage Types - Electronic

10.3.2 Local Data Storage Types - Electronic

1.0 * **Where is the electronic data being stored? Select all that apply.**

VAPHS Network (shared drive)

If "Other" please describe OR if you would like to provide additional information for clarification, please elaborate in the text box below.

If you selected VAPHS or VA Network (Shared Drive), please provide the name of the drive (i.e. "MySharedDriveName (\\vapthshsare) (X:)"):

VHAPTHIbinsJ$ (\\vhapthshare) (N:)

ID: Pro00000878 View: 10.4.0 Data Security and Privacy: Reusing Data

10.4.0 Data Security and Privacy: Reusing Data

1.0 * **Will the data collected in this study be reused in other studies?** ○ Yes ◉ **No**

If yes, please describe where the data to be reused will be stored and how access to that data will be provided and monitored:

2.0 **If this research is part of a grant, please upload the Data Management Access Plan (DMAP) or Resource Sharing Plan for this study.**

Name	Modified Date
There are no items to display	

ID: Pro00000878 View: 10.6.0 Data Security and Privacy: HIPAA

10.6.0 Data Security and Privacy: HIPAA

The Healthcare Insurance Portability and Accountability Act (HIPAA) prohibits the use of a person's Protected Health Information without a valid authorization.

1.0 * **Select the option which fits this study:**

Name
○ Not applicable: No PHI is being used or disclosed by VAPHS
○ Not applicable: Waiver has been requested
○ HIPAA Authorization (Combined Consent and HIPAA Authorization)
◉ **HIPAA Authorization (Standalone)**

Upload HIPAA authorization (Standalone) here:

Document	Modified Date	Version Number
View Ibinson HIPPA Auth 04-25-14.doc(0.06)	5/5/2016 11:13 AM	0.06

2.0 **At screening will clinical personnel be asked to share potential participants PHI:**

○ Yes ◉ **No**

If yes, please upload the 10-5345:

ID: Pro00000878 View: 10.7.0 Data Security and Privacy: Additional Information

10.7.0 Data Security and Privacy: Additional Information

1.0 **Does this research involve...**

* **...specially obtained software?** (●) **Yes** ( ) No

If yes, please describe the software and what it is being used for:
IBM SPSS will be used for statistical analysis.

* **...one or more Web-based applications?** ( ) Yes (●) **No**

If yes, please describe the application and what it is being used for:

* **...mobile devices?** ( ) Yes (●) **No**

If yes, please describe:

2.0 * **Will a Certificate of Confidentiality be obtained for this study?** ( ) Yes (●) **No**

If yes, please attach the Certificate of Confidentiality:

3.0 * **Will VA sensitive information be transported and utilized outside protected environments?** ( ) Yes (●) **No**

If you answered yes above, please upload a fully executed VAPHS Memo to Take VA Sensitive Information Outside a Protected Environment by following **these instructions** .

ID: Pro00000878 View: 10.8.0 Data Security and Privacy: Certifications

10.8.0 Certifications

1.0 * **I certify that all study staff are up-to-date and will remain up-to-date with Information Security Awareness Training, Rules of Behavior, and VHA Privacy Training.**
(●) **Yes** ( ) No

2.0 * **I also certify that when an individual is no longer part of the study team, access will be removed to research study data.** (●) **Yes** ( ) No

3.0 * **I certify that all research records will be maintained in accordance with the Veterans Health Administration (VHA)Records Control Schedule. Paper records will be disposed of using methods deemed appropriate by the VAPHS Privacy Officer, and all electronic data will be sanitized using methods rendered appropriate by the VAPHS ISO.** (●) **Yes** ( ) No

4.0 * **I certify that any loss or compromise of any VA sensitive information (including research data), VA equipment or device, or any non-VA equipment or device that is used to transport, access, or store VA information will be reported in accordance with the reporting requirements outlined in VA Handbook 6500.** (●) **Yes** ( ) No

5.0 * **I certify that, in accordance with VA Handbook 6500, no personal laptops will be used for official VA business in conjunction with this study.** (●) **Yes** ( ) No

ID: Pro00000878 View: 11 Local Data Safety Monitoring Plan

Local Data Safety Monitoring Plan

For local studies, a data and safety monitoring plan (DSMP) must be established.

1.0 * **Please describe how the study procedures and data being collected will be continuously monitored so that changes in the risk/benefit ratio can be determined in a timely fashion during the course of the study:**

A data and safety monitoring plan will be implemented to ensure that there are no changes in the benefit/risk ratio during the study and that confidentiality of research data is maintained. Any instances of adverse events, protocol deviations, or other problems identified during the meetings will be reported as soon as possible within the required reporting timeframes using the standard forms and procedures set forth by the IRB. Events will be monitored and discussed during study team meetings and entered into the data collection system. Cumulative reports will be submitted yearly with IRB renewal.

2.0 * **Describe how frequently Investigators, study personnel, and the clinical coordinators involved in the study will meet and/or review study data.**

The investigators will meet every four months to discuss the study progress and data analysis and address any issues or concerns at the time. These meetings will be overseen by James Ibinson, the study PI.

3.0 * **Will this study use a Data Safety Monitoring Board or Data Monitoring committee?**

○ Yes ◉ **No**

4.0 * **Will this study use a Medical Monitor?**

○ Yes ○ No

ID: Pro00000878 View: 12 Costs and Payments

Costs and Payments

1.0 * **Does this study have a budget?:**

○ Yes ◉ **No**

If yes, please upload the current budget:

2.0 * **Will patients receive payments for this study?**

○ Yes ◉ **No**

If yes, please upload the financial letter of support (either from the Business Service line or the Veterans Health Foundation) or documentation waiving the requirement of a letter of support:
There are no items to display

3.0 * **Are you paying patients using the WePay system?**

not applicable

ID: Pro00000878 View: 12.1 Costs

Costs

1.0 * **Will subjects be required to pay for any services outside of the VHA that may be required as part of participating in this research study?**
No

ID: Pro00000878 View: 14 References

References:

1.0 * **Please provide a list of references** *(Multi-site protocols: You may reference the page numbers in the original protocol):*

1) Aasvang E, Kehlet H. Chronic postoperative pain: the case of inguinal herniorrhaphy. Br J Anaesth 2005; 95: 69-76

2) Cunningham J, Temple WJ, Mitchell P, Nixon JA, Preshaw RM, Hagen NA. Cooperative hernia study. Pain in the post-repair patient. Ann Surg 1996; 224: 598-602

3) Cornell RB, Kerlakian GM. Early complications and outcomes of the current technique of transperitoneal laparoscopic herniorraphy and a comparison to the traditional open approach. Am J Surg 1994; 168: 275-9

4) Searle RD, Simpson MP, Simpson KH, Milton R, Bennett MI. Can chronic neuropathic pain following thoracic surgery be predicted during the postoperative period? Interact Cardiovasc Thorac Surg 2009 Dec; 9(6): 999-1002

5) Desborough JP. The stress response to trauma and surgery. Br J Anaesth 2000; 85: 109-17

6) Ledowski T, Bein B, Hanss R, Paris A, Fudickar W, Scholz J, Tonner PH. Neuroendocrine stress response and heart rate variability: a comparison of total intravenous versus balanced anesthesia. Anesth Analg 2005 Dec;101(6):1700-5

7) El-Tahan MR, Warda OM, Diab DG, Ramzy EA, Matter MK. A randomized study of the effects of perioperative i.v. lidocaine on hemodynamic and hormonal responses for cesarean section. J Anesth 2009; 23(2): 215-21

8) A. R. H Twijnstra, A. Dahan, M. M. ter Kuile, F. W. Jansen. Nociceptive and stress hormonal state during abdominal, laparoscopic, and vaginal hysterectomy as predictors of postoperative pain perception. Gynecological Surgery 2013; 10(1): 45-50

9) Huiku M, Uutela K, van Gils M, Korhonen I, Kymalainen M, Merilainen P, Paloheimo1 M, Rantanen M, Takala P, Viertio-Oja H, Yli-Hankala A. Assessment of surgical stress during general anaesthesia. Br J Anaesth 2007; 98: 477-55

10) Macrae WA. Chronic pain after surgery. Br J Anaesth 2001; 87: 88–98

11) Chang L, Ma T, Tsay S, Jong G. Relationships between pain intensity and heart rate variability in patients after abdominal surgery: a pilot study. Chin Med J 2012;125(11):1964-1969

ID: Pro00000878 View: 15 Miscellaneous Documents

Miscellaneous Documents

If you have any documents that need to be included in this submission, but do not fit in any of the previous sections please upload them here.

	Document	Description	Version Number
View	Cover Letter for Mailed Consent Forms(0.01)		0.01
View	Ibinson CV(0.01)		0.01

ID: Pro00000878 View: SF - Final Page

Final Page

You have completed your application!

Please hit "Finish" to save and exit the application. Doing so will NOT submit the application for review.

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must press the "SUBMIT STUDY" button in My Activities for this Study ID:Pro00000878.

You can track the ongoing status of your submission by logging into the study workspace.

Please feel free to contact the IRB with any questions or concerns.

ID: Pro00000878

View: Drugs used in study

All Drugs: REMIFENTANIL

Name Of Drug if Other:

* **Manufacturer of Drug:** Mylan Institutional

* **Is the drug, biological or nutrional (e.g. herbal or dietary) supplements FDA approved?** ◉ **Yes** ○ No

* **IND Holder:** Not Investigational

IND Number:

☒ Fields on this page show drug entry by SELECTION in addition to a "type in the drug" model.

Please provide any additional information about the drug being used for this study:

The use of this drug is considered standard of care for use during the maintenance of general anesthesia. Its use in this study is for an FDA approved indication.

ID: Pro00000878

View: Drugs used in study

	All Drugs:	KETAMINE
	Name Of Drug if Other:	
*	**Manufacturer of Drug:**	JHP Pharmaceuticals
*	**Is the drug, biological or nutrional (e.g. herbal or dietary) supplements FDA approved?**	(•) **Yes** ( ) No
*	**IND Holder:**	Not Investigational
	IND Number:	

☒ Fields on this page show drug entry by SELECTION in addition to a "type in the drug" model.

Please provide any additional information about the drug being used for this study:

The use of this drug is considered standard of care for use during the maintenance of general anesthesia. Its use in this study is for an FDA approved indication.

ID: Pro00000878

View: Drugs used in study

	All Drugs:	PROPOFOL
	Name Of Drug if Other:	
*	**Manufacturer of Drug:**	APP Pharmaceuticals
*	**Is the drug, biological or nutrional (e.g. herbal or dietary) supplements FDA approved?**	(•) **Yes** ( ) No
*	**IND Holder:**	Not Investigational
	IND Number:	

☒ Fields on this page show drug entry by SELECTION in addition to a "type in the drug" model.

Please provide any additional information about the drug being used for this study:

The use of this drug is considered standard of care for the induction and maintenance of general anesthesia. Its use in this study is for an FDA approved indication.

ID: Pro00000878

View: Drugs used in study

All Drugs: SEVOFLURANE

Name Of Drug if Other:

* **Manufacturer of Drug:** AbbVie Inc.

* **Is the drug, biological or nutrional (e.g. herbal or dietary) supplements FDA approved?** (●) **Yes** ( ) No

* **IND Holder:** Not Investigational

IND Number:

☒ Fields on this page show drug entry by SELECTION in addition to a "type in the drug" model.

Please provide any additional information about the drug being used for this study:

The use of this drug is considered standard of care for the induction and maintenance of general anesthesia. Its use in this study is for an FDA approved indication.

ID: Pro00000878

View: Drugs used in study

All Drugs: LIDOCAINE HCL

Name Of Drug if Other:

* **Manufacturer of Drug:** B Braun

Fields on this page show drug entry by SELECTION in addition to a "type in the drug" model.

* **Is the drug, biological or nutrional (e.g. herbal or dietary) supplements FDA approved?** (●) **Yes** ( ) No

* **IND Holder:** Not Investigational

IND Number:

Please provide any additional information about the drug being used for this study:

The use of this drug is considered standard of care for use during the maintenance of general anesthesia. Its use in this study is for an FDA approved indication.

ID: Pro00000878 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Remifentanyl administration

Common Risks:

Infrequent Risks:
Nausea/vomiting, hypotension, bradycardia.

Other Risks:

ID: Pro00000878 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Ketamine administration

Common Risks:

Infrequent Risks:
Hypertension, tachycardia, respiratory depression, nystagmus, rash, confusion, hallucinations, delirium.

Other Risks:

ID: Pro00000878 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Patient Survey

Common Risks:
None.

Infrequent Risks:

Other Risks:
Very rare risk for a breach of confidentiality. All hard-copy records pertaining to patient involvement in this research study will be stored in a locked file cabinet in the PI's Anesthesia Service Office. All computerized records pertaining to patient involvement in this research study are secured in government-approved VAPHS databases and servers. Patient identity on these records will be indicated by a case number. This information will only be accessible to the investigators and their research study staff.

ID: Pro00000878 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Sevoflurane

Common Risks:

Infrequent Risks:
Hypotension, bradycardia, somnolence, agitation, nausea/vomiting, cough.

Other Risks:

ID: Pro00000878 View: Risk Detail Entry

Address for each screening procedure, research intervention/interatction, and follow-up/monitoring procedure:

* Research Activity:
Propofol adminstration

Common Risks:

Infrequent Risks:
Apnea, hypotension, burning/stinging pain on injection, rash, dizziness, agitation, delirium.

Other Risks: