University of California, Los Angeles

Research Protocol

Pudendal Enhancement of ERAS for Reconstructive Surgery (PEERS study)

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LIST OF ABBREVIATIONS

Add all other abbreviations referenced in the protocol and delete any not referenced in the protocol.

AE	adverse event
ERAS	Enhanced recovery
CFR	Code of Federal Regulations
CRF	Case Report Form
DMC	Data Monitoring Committee
DSMB	Data Safety Monitoring Board
EBL	Estimated blood loss
FDA	Food and Drug Administration
FPMRS	Female Pelvic Medicine and Reconstructive Surgery
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
IV	Intravenous
mg	Milligram
mcg	microgram
ml	Milliliters
MME	Medical morphine equivalent
NSAID	Nonsteroidal anti-inflammatory drugs
NRS	Numeric rating scale
PI	Principal Investigator
PO	Per os (oral administered medication)
PNB	Pudendal nerve block

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1.0 PROTOCOL SUMMARY AND/OR SCHEMA

Pudendal Enhancement of ERAS for Reconstructive Surgery (PEERS study)
To determine whether administration of a PNB at time of vaginal reconstructive surgery can reduce use of narcotics and reported pain scores in the immediate postoperative period within the setting of multimodal postoperative pain control of ERAS. Women >18yo undergoing vaginal reconstructive surgery without a hysterectomy will be randomized to either standard of care with typical use of local anesthetic during their surgery versus perioperative PNB in addition to typical use of local anesthetic during their surgery. PNB will be performed with 0.5% bupivacaine with 10cc injected each on the left and right side. All patients will be on a standard preoperative and postoperative multimodal pain regimen. Patients will be followed until 6 weeks after surgery.

2.0 OBJECTIVES AND SCIENTIFIC AIMS

- Narcotic use measured in MME at 24 hours after surgery
- Narcotic use measure in MME at 48 hours after surgery
- Average pain score by NRS at 0-2 hours after surgery
- Average pain score by NRS at 2-4 hours after surgery
- Average pain score by NRS at 4-8 hours after surgery
- Average pain score by NRS at 8-12 hours after surgery
- Average pain score by NRS at 12-24 hours after surgery
- Pain score by NRS at 24 hours after surgery
- Pain score by NRS at 48 hours after surgery
- Time to return to normal daily activities in days
- Operative time in minutes
- EBL in ml
- Rate of urinary retention requiring catheter >48 hours after surgery
- Length of hospital stay in hours
- Patient satisfaction with postoperative recovery at 48 hours after surgery
- Patient satisfaction with postoperative recovery at 2 weeks after surgery
- Patient satisfaction with postoperative recovery at 6 weeks after surgery

3.0 BACKGROUND AND RATIONALE

The United States is currently in the midst of an opioid crisis. Opioid overdoses account for over 130 deaths a day in the United States[1]. One of the movements in health care to

reduce opioid use has included the adoption of the Enhance Recovery After Surgery (ERAS) protocol. ERAS employs a multimodal approach to pain medication by relying on scheduled nonsteroidal anti-inflammatory drugs (NSAIDS) and acetaminophen with supplemental use of opioid as needed. Additionally, ERAS protocol has been shown to improve patient outcomes. Studies in Gynecologic Oncology and general Gynecology have demonstrated adoption of ERAS leads to reducing in cost and opioid use as well as increase in patient satisfaction.[2-6]

One component of ERAS is utilizing regional anesthesia and local nerve blocks for intraoperative pain control and reduce or prevent the afferent stimulus of pain.[4,5,8-10] Local anesthesia is commonly used in vaginal reconstructive surgery. Its use has been employed as an adjunct for pain control with either regional or general anesthesia and as a technique for further dissection of tissue planes intraoperatively. Infiltration is typically done with lidocaine or bupivacaine. Peripheral nerve blocks have also been used in vaginal reconstructive surgery including paracervical block and pudendal nerve block (PNB). Numerous studies have demonstrated feasibility of vaginal reconstructive surgery using local anesthesia with and without pudendal nerve block and sedation instead of general anesthesia for intraoperative pain control.[11-17]

The pudendal nerve arises from S2, S3, S4 nerve roots and carries sensory function to the lower vagina, vulva, and perineum. PNB can be readily performed in a transvaginal or transperineal manner at time of vaginal surgery. This has more commonly been employed during the second stage of labor for local anesthesia, but its use has also been described in vaginal reconstructive surgery.[16,18-21] Typically, PNB at time of vaginal surgery is performed with bupivacaine or lidocaine. The results from these studies are mixed. The studies looking at PNB use in anterior and/or posterior vaginal wall repairs have demonstrated reduced pain and narcotic medication use in the immediate postoperative period compared to no PNB under general anesthesia[20] and PNB as sole anesthesia with sedation compared to general anesthesia.[19] One study, though, demonstrated no difference in pain scores or narcotic medication consumption with use of PNB in vaginal reconstructive surgery compared to sham PNB with saline. However, this study routinely used PCA for patients postoperatively[18], which is not current standard of care. The available data is limited and heterogenous in type of reconstructive surgeries performed, type of anesthesia used, medication in PNB, and administration route of PNB. Despite the one study demonstrated no difference[18], the literature on PNB and vaginal reconstructive surgery suggest feasibility with possible improvement in postoperative

pain and reduction in postoperative narcotic use with little risk.[16,18-21] PNB has a low risk of complications. Complications theoretically include hematoma formation, infection, or systemic toxicity.[22]

Our aim with this study is to determine if PNB improves patients' postoperative pain control and reduces their need for supplemental opioid pain medication after vaginal reconstructive surgery. Additionally, we want to examine if use of the PNB has a significant impact on patient satisfaction with their postoperative care in the setting of ERAS.

4.0 OVERVIEW OF STUDY DESIGN/INTERVENTION

4.1 Design

This will be a prospective blinded randomized controlled trial. We will recruit women who are undergoing vaginal prolapse repair surgery with a Female Pelvic Medicine and Reconstructive Surgery fellowship-trained provider within the UCLA Health System.

Women will be recruited prior to undergoing vaginal reconstructive surgery. They will then be randomized to control group with standard of care with local anesthesia used during surgery (Group 1) or PNB in addition to use of local anesthesia typically used during surgery (Group 2).

All pain medication will be standardized. Preoperative medications per our ERAS protocol will include oral acetaminophen 1000mg, gabapentin 600mg, and celecoxib 400mg. During surgery the patient will undergo their randomized intervention as either Group 1 or Group 2. Postoperative medications per our ERAS protocol include scheduled acetaminophen 650mg PO every 6 hours and ketorolac 30mg IV every 6 hours. For patients 65 years or older they will have a modified protocol and will receive ketorolac 15mg IV every 6 hours.[23] For supplemental pain medication patients will have the following available: tramadol 50mg PO every 6 hours as needed for moderate pain (pain 4-6/10 on NRS scale), tramadol 100mg PO every 6 hours as needed for severe pain (pain 7-10/10 on NRS scale), and oxycodone 5mg PO every 4 hours as needed for breakthrough pain as supplemental pain medication. If the above regimen does not allow for sufficient pain control then additional hydromorphone IV 0.2mg or morphine IV 2mg can be ordered by the provider as needed, but these medications will not be standard in the postoperative order set. The providers will know what intervention the patients

underwent, but the patients and the nursing care team obtaining pain scores in the hospital will be blinded to the intervention.

The patients' pain scores on the numeric rating scale (NRS) and supplemental opioid use measured in morphine milligram equivalent (MME) will be tracked during their hospitalization, which is typically a 23-hour observation. They will then be called at 48 hours for further follow-up on pain score by NRS and asked how much pain medication they have taken since leaving the hospital and their overall satisfaction with their pain control. To help with the determination of supplemental pain medication used and pain scores, the patients will be provided a worksheet upon discharge that outlines their recommended medication routine, allows them to record their supplemental opioid medication use with dose and time, and also provides space for them to record their pain score at 24 and 48 hours post operatively. The patient will then be contacted at 2 weeks after surgery to determine if they have returned to normal activities (walking, sitting, and performing daily household tasks comfortably) and if so at what point this occurred, as well as their overall satisfaction with their postoperative pain control again. The two week contact will be either a phone call or clinic visit depending on the provider's preference for patient follow-up. The last point of contact will be at 6 weeks to determine time to return to normal activities, if they had not met this milestone at the 2-week contact, and again assess their overall satisfaction with their postoperative pain control.

4.2 Intervention

The intervention will be a PNB with bilateral injection of 10cc each of 0.5% bupivacaine without epinephrine. The surgeons will still be able to use local anesthetic as they usually would during the surgery, but there will be a limitation on the total amount of local anesthesia that can be administered based on pharmacologic guidelines.[24] During vaginal reconstructive surgery, local infiltration is typically performed with 0.25% or 0.5% bupivacaine with epinephrine. The maximum dose for this medication is 175mg total without epinephrine and 225mg with epinephrine 1:200,000.[24] To err on the side of caution, the maximum dose allowed would be based on the maximum dose without epinephrine which is a total of 35ml of 0.5% bupivacaine or 70ml of 0.25% bupivacaine. Because the intervention of PNB will be with 20ml of 0.5% bupivacaine, the remaining local anesthetic that can be used is 15ml of 0.5% bupivacaine or 30ml of 0.25% bupivacaine. If 1% lidocaine is the local anesthetic of choice by the provider then an

additional 21cc maximum can be used based on total maximum doses of each medication.

5.0 CRITERIA FOR SUBJECT ELIGIBILITY

Describe the characteristics of the subject population.

5.1 Subject Inclusion Criteria

- Female
- Age > 18 years old
- English speaking
- Undergoing vaginal reconstructive surgery of at least 2 compartments (anterior vaginal wall, posterior vaginal wall, and/or apical suspension including hysteropexy, uterosacral ligament suspension, or sacrospinous ligament fixation)

5.2 Subject Exclusion Criteria

- Hysterectomy at time of surgery—is variable in duration which may affect response to PNB
- Inability to tolerate opioids—allergy or medical contraindication
- Inability to tolerate local anesthetic agents—allergy or medical contraindication
- Inability to tolerate NSAIDS—allergy or medical contraindication
- Inability to tolerate acetaminophen—allergy or medical contraindication
- Coagulation disorder
- Chronic pain syndrome using opioid medication on a regular basis prior to surgery

6.0 RECRUITMENT PLAN

Subjects will be recruited to the study if they are scheduled for a vaginal reconstructive surgery by an FPMRS-trained provider. This may be at the time of preoperative counseling in the clinic or prior to surgery either with a phone call in the time leading up to surgery or once they have checked into the hospital or surgery center for their scheduled procedure. Only women will be recruited for the study as the surgery is limited to a female population. Recruitment will be performed despite race with the goal of having all minorities represented in the study.

If initial contact is done in person the patients will be provided with a copy of the informed consent and it will be reviewed in detail with them. If the initial contact is over the phone, we will verbally discuss the consent and all aspects of the study and bring the

consent form to them in the preoperative area prior to surgery and offer to have them pick it up from clinic at their convenience prior to that date as well.

7.0 ASSESSMENT/EVALUATION PLAN

- NRS: scale of 0-10 to have patient's indicate their level of pain with 0 indicating "no pain" and 10 indicating "worst possible pain"
- Satisfaction scale—5-point scale Likert scale
  - 1 = Very satisfied
  - 2 = Somewhat satisfied
  - 3 = Neither satisfied or dissatisfied
  - 4 = Somewhat dissatisfied
  - 5 = Very dissatisfied
- Return to normal activities—defined as "walking, sitting, and performing daily household tasks comfortably"
- Opioid conversion to MME
  - Review MAR for first 24 hours/hospitalization
  - Review MAR and ask via phone call for 24-48 hours after surgery (patients will have worksheet to record what supplemental pain medication they have taken since discharge)
  - Conversion factors are[25,26]:
    - Fentanyl IV/IM (mcg) MME conversion 0.3
    - Hydromorphone IV (mg) MME conversion 20
    - Morphine IV (mg) MME conversion 3
    - Oxycodone PO (mg) MME conversion 1.5
    - Tramadol PO (mg) MME conversion 0.1

8.0 TOXICITIES/SIDE EFFECTS

PNB has a low risk of complications. Complications theoretically include hematoma formation, infection, or systemic toxicity.[22] In recent papers using PNB in vaginal reconstructive surgery there have been no reported incidences of any of the above adverse effects.[14,18,19]

8.1 Adverse Events

An adverse event (AE) is any untoward medical occurrence in a clinical investigation of a patient administered a pharmaceutical product and that does not necessarily have a causal relationship with the treatment. An AE is therefore any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the administration of an investigational product, whether or not related to that investigational product. An unexpected AE is one of a type not identified in nature, severity, or frequency in the current Investigator's Brochure or of greater severity or frequency than expected based on the information in the Investigator's Brochure.

The Investigator will query, via discussion with the subject, for the occurrence of AEs during each subject visit and record the information in the site's source documents. Adverse events will be recorded in the patient CRF. Adverse events will be described by duration (start and stop dates and times), severity, outcome, treatment and relation to study drug, or if unrelated, the cause.

Table 1. AE Severity Grading

Severity (Toxicity Grade)	Description
Mild (1)	Transient or mild discomfort; no limitation in activity; no medical intervention or therapy required. The subject may be aware of the sign or symptom but tolerates it reasonably well.
Moderate (2)	Mild to moderate limitation in activity, no or minimal medical intervention/therapy required.
Severe (3)	Marked limitation in activity, medical intervention/therapy required, hospitalizations possible.
Life-threatening (4)	The subject is at risk of death due to the adverse experience as it occurred. This does not refer to an experience that hypothetically might have caused death if it were more severe.

Table 2. AE Relationship to Study Drug

Relationship to Drug	Comment
Definitely	Previously known toxicity of agent; or an event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to the suspected drug; that is confirmed by stopping or reducing the dosage of the drug; and that is not explained by any other reasonable hypothesis.
Probably	An event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to the suspected drug; that is confirmed by stopping or reducing the dosage of the drug; and that is unlikely to be explained by the known characteristics of the subject's clinical state or by other interventions.
Possibly	An event that follows a reasonable temporal sequence from administration of the drug; that follows a known or expected response pattern to that suspected drug; but that could readily have been produced by a number of other factors.
Unrelated	An event that can be determined with certainty to have no relationship to the study drug.

8.2 Serious Adverse Events

An SAE is defined as any AE occurring at any dose that results in any of the following outcomes:

- death
- a life-threatening adverse experience
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant disability/incapacity
- a congenital anomaly/birth defect

Other important medical events may also be considered an SAE when, based on appropriate medical judgment, they jeopardize the subject or require intervention to prevent one of the outcomes listed.

8.2.1 Serious Adverse Event Reporting

Study sites will document all SAEs that occur (whether or not related to study drug) per UCLA OHRPP Guidelines. The collection period for all SAEs will begin after informed consent is obtained and end after procedures for the final study visit have been completed.

In accordance with the standard operating procedures and policies of the local Institutional Review Board (IRB)/Independent Ethics Committee (IEC), the site investigator will report SAEs to the IRB/IEC.

9.0 PRIMARY OUTCOMES

The primary outcome is the amount of supplemental pain medication (narcotic pain medication) used in the first 24 hours after surgery in oral morphine milligram equivalents (MME). This will be obtained from review of the medical chart in Care Connect and calculating all supplemental pain medication used including: tramadol, oxycodone, fentanyl, hydromorphone, and morphine.

10.0 CRITERIA FOR REMOVAL FROM STUDY

Subjects will be removed from the study if their postoperative pain regimen needs to be modified from the standard protocol. This may be due to poorly controlled pain or unexpected toxicities/side effects from the medication. Additionally, subjects will be removed from study if researchers are unable to contact for appropriate follow-up via telephone or clinic visit. The subject always has the right to withdraw consent for continued participation. Lastly, death of the subject would lead to removal from the study.

11.0 BIOSTATISTICS

The planned design of minimum 19 patients per arm of control group vs pudendal nerve block provides 80% power to detect a difference in mean supplemental pain medication use of 5.57 morphine milligram equivalents (MME) at 24 hours after surgery. This assumes a two-sample t-test with a standard deviation of supplemental pain medication use of 4.61-6.87 MME (based on Ismail et al 2012), and an alpha of 0.05. With an anticipated 15% rate of loss to follow-up we will plan to recruit 22 patients per arm. This sample size also allows for the detection of a 20% reduction in mean pain scores at 24 hours with a standard deviation between 0.74-1.32 (based on Ismail et al 2012).

For reference 5.57 MME is 55.7mg of Tramadol and 8.36mg of Oxycodone.

Patients will be randomized to either control or PNB by a randomization protocol as described in section 12.2.

12.0 RESEARCH PARTICIPANT REGISTRATION AND RANDOMIZATION PROCEDURES

12.1 Research Participant Registration

Obtain informed consent, by following procedures defined in section entitled Informed Consent Procedures. An Eligibility Checklist will be completed and relevant source documentation will be maintained with the checklist and reviewed by the Principal Investigator prior to registration.

12.2 Randomization

The randomization assignments will be generated by the principal statistician in the UCLA Department of Urology with a random number generator algorithm in Microsoft Excel or SAS so that the 44 proposed recruited patients will be randomly assigned to control or intervention group in an equal amount of 22 per group. This will be stored in a central location on a password protected system on the UCLA Health Box for the research staff to access and as each patient is randomized they will use the next available group assignment on the sheet and cross them off. This will be closely monitored to maintain appropriate use. The randomization will occur on day of surgery.

13.0 DATA COLLECTION, RETENTION AND MONITORTING

13.1 Data Collection Instruments

The Investigator will prepare and maintain adequate and accurate source documents designed to record all observations and other pertinent data for each subject treated with the study drug.

Study personnel will enter data from source documents corresponding to a subject's visit into the protocol-specific electronic Case Report Form (eCRF) OR paper CRF, when the information corresponding to that visit is available. Subjects will have identifiers within the study database, but all information will be de-identified at time of analysis. Paper CRF will have patient identifiers, but will be stored in a secure location that is only accessible by study personnel.

For eCRFs: If a correction is required for an eCRF, the time and date stamps track the person entering or updating eCRF data and creates an electronic audit trail. *For paper CRFs:* If a correction is made on a CRF, the study staff member will line through the incorrect data, write in the correct data and initial and date the change.

The Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of this study must be reviewed and verified for completeness and accuracy by the Investigator. A copy of the CRF will remain at the Investigator's site at the completion of the study.

13.2 Data Management Procedures

The data will be entered into a validated database of REDCap. Database lock will occur once quality assurance procedures have been completed. All procedures for the handling and analysis of data will be conducted using good computing practices meeting FDA guidelines for the handling and analysis of data for clinical trials.

13.3 Data Quality Control and Reporting

After data have been entered into the study database, a system of computerized data validation checks will be implemented and applied to the database on a regular basis. The study database will be updated in accordance with the resolved queries. All changes to the study database will be documented.

13.4 Archival of Data

The REDCap database is safeguarded against unauthorized access by established security procedures; appropriate backup copies of the database and related software files will be maintained. Databases are backed up by the database administrator in conjunction with any updates or changes to the database.

At critical junctures of the protocol (e.g., production of interim reports and final reports), data for analysis is locked and cleaned per established procedures.

13.5 Availability and Retention of Investigational Records

The Investigator must make study data accessible to the WHCRU monitor, , IRB/IEC, and Regulatory Agency (e.g., FDA) inspectors upon request. A file for each subject must be maintained that includes the signed Informed Consent, HIPAA Authorization and Assent Form and copies of all source documentation related to that subject. The Investigator must ensure the reliability and availability of source documents from which the information on the CRF was derived.

All study documents (patient files, signed informed consent forms, eligibility checklists, copies of CRFs, Study File Notebook, etc.) must be kept secured for a period of two years following marketing of the investigational product or for two years after centers

have been notified that the IND has been discontinued. There may be other circumstances for which the Sponsor is required to maintain study records and, therefore, the Sponsor should be contacted prior to removing study records for any reason.

13.6 Monitoring

Monitoring visits will be conducted by representatives of the Women's Health Clinical Research Unit.

13.7 Subject Confidentiality

In order to maintain subject confidentiality, CRFs will only be accessible by study personnel given identifiers will be on source documentation. They will be maintained in locked cabinet. Additionally, all electronic documentation will be within the REDCap database which is safeguarded against unauthorized access by established security procedures.

14.0 ADMINISTRATIVE, ETHICAL, REGULATORY CONSIDERATIONS

The study will be conducted according to the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Obligations of Clinical Investigators (21 CFR 312).

To maintain confidentiality all study records will be kept in a locked file cabinet. Identifiers will be removed and patient data will be coded at the time of analysis. The linking list will be maintained separately and then destroyed after publications. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by the FDA. The Investigator must also comply with all applicable privacy regulations (e.g., Health Insurance Portability and Accountability Act of 1996, EU Data Protection Directive 95/46/EC).

14.1 Protocol Amendments

Any amendment to the protocol will be written by Dr. Tamara Grisales. Protocol amendments cannot be implemented without prior written IRB/IEC approval except as necessary to eliminate immediate safety hazards to patients. A protocol amendment intended to eliminate an apparent immediate hazard to patients may be implemented immediately, provided the IRBs are notified within five working days.

14.2 Institutional Review Boards and Independent Ethics Committees

The protocol and consent form will be reviewed and approved by the IRB/IEC of each participating center prior to study initiation. Serious adverse experiences regardless of

causality will be reported to the IRB/IEC in accordance with the standard operating procedures and policies of the IRB/IEC, and the Investigator will keep the IRB/IEC informed as to the progress of the study. The Investigator will obtain assurance of IRB/IEC compliance with regulations.

Any documents that the IRB/IEC may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator's Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB/IEC. The IRB/IECs written unconditional approval of the study protocol and the informed consent form will be in the possession of the Investigator before the study is initiated. The IRB/IECs unconditional approval statement will be transmitted by the Investigator to the Sponsor or designee prior to the shipment of study supplies to the site. This approval must refer to the study by exact protocol title and number and should identify the documents reviewed and the date of review. Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the patients or when the change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB/IEC and written verification that the modification was submitted and subsequently approved should be obtained.

The IRB/IEC must be informed of revisions to other documents originally submitted for review; serious and/or unexpected adverse experiences occurring during the study in accordance with the standard operating procedures and policies of the IRB; new information that may affect adversely the safety of the patients of the conduct of the study; an annual update and/or request for re-approval; and when the study has been completed.

14.3 Informed Consent Form

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Investigator will prepare the informed consent form, assent and HIPAA authorization and provide the documents to the Sponsor or designee for approval prior to submission to the IRB/IEC. The consent form generated by the Investigator must be acceptable to the Sponsor and be approved by the IRB/IEC. The written consent document will embody the elements of informed consent as described in the International Conference on

Harmonisation and will also comply with local regulations. The Investigator will send an IRB/IEC-approved copy of the Informed Consent Form to the Sponsor (or designee) for the study file.

A properly executed, written, informed consent will be obtained from each subject prior to entering the subject into the trial. Information should be given in both oral and written form and subjects (or their legal representatives) must be given ample opportunity to inquire about details of the study. If appropriate and required by the local IRB/IEC, assent from the subject will also be obtained. If a subject is unable to sign the informed consent form (ICF) and the HIPAA authorization, a legal representative may sign for the subject. A copy of the signed consent form (and assent) will be given to the subject or legal representative of the subject and the original will be maintained with the subject's records.

14.4 ClinicalTrials.gov

ClinicalTrials.gov is a website that provides information about federally and privately supported clinical trials. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify the subject. At most, the website will include a summary of the results.

15.0 PUBLICATIONS

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a UCLA guidelines. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996.

16.0 INVESTIGATOR RESPONSIBLITIES

By signing the Agreement of Investigator form, the Investigator agrees to:

1. Conduct the study in accordance with the protocol and only make changes after notifying the Sponsor (or designee), except when to protect the safety, rights or welfare of subjects.
2. Personally conduct or supervise the study (or investigation).
3. Ensure that the requirements relating to obtaining informed consent and IRB review and approval meet federal guidelines, as stated in § 21 CFR, parts 50 and 56.
4. Report to the Sponsor or designee any AEs that occur in the course of the study, in accordance with §21 CFR 312.64.

5. Ensure that all associates, colleagues and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.
6. Maintain adequate and accurate records in accordance with §21 CFR 312.62 and to make those records available for inspection with the Sponsor (or designee).
7. Ensure that an IRB that complies with the requirements of §21 CFR part 56 will be responsible for initial and continuing review and approval of the clinical study.
8. Promptly report to the IRB and the Sponsor (or designee) all changes in the research activity and all unanticipated problems involving risks to subjects or others (to include amendments and IND safety reports).
9. Seek IRB approval before any changes are made in the research study, except when necessary to eliminate hazards to the patients/subjects.
10. Comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements listed in § 21 CFR part 312.

17.0 REFERENCES

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18.0 APPENDICES

APPENDIX 1. SCHEDULE OF STUDY VISITS

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	VISIT 1 (PREOPERATIVE COUNSELING VISIT, CLINIC OR PREOPERATIVE AREA)[a]	VISIT 2 (48 HOURS AFTER SURGERY) PHONE CALL	VISIT 3 (2 WEEKS AFTER SURGERY) PHONE CALL OR CLINIC VISIT	VISIT 4 (6 WEEKS AFTER SURGERY) CLINIC VISIT
Informed Consent	X			
Medical History	X			
Complete Physical Exam	X			
Abbreviated Physical Exam				
Height	X			
Weight	X			
Vital Signs	X			
Home Medication Review	X			
Numeric pain scale assessment		X		
Amount of supplemental pain medication used		X		
Return to daily activities			X	X
Satisfaction with postoperative care		X	X	X
Adverse Experiences		X	X	X

[a] ±2 days