Title: Ultrasound Guided Local Infiltration Analgesia for Hip Arthroscopy

PI: Sanjay K. Sinha, MD

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Ultrasound Guided Local Infiltration Analgesia for Hip Arthroscopy Protocol

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Table of Contents:

1.0 Background

Patients undergoing hip arthroscopy experience moderate to severe postoperative pain. Effective pain control after surgery is an important component in the overall management of these patients. Good pain control encourages early participation in rehabilitation program, increases success of the surgery, and improves patient satisfaction. Typically, postoperative analgesia is provided to these patients either with nerve blocks (psoas compartment lumbar plexus block and sciatic nerve block) or opioid medications [1,2,3]. Both these methods provide good pain relief but nerve blocks are associated with weakness of lower extremity muscles which interferes with early ambulation and increase the risk of falls while narcotic medications increase the risk of nausea, vomiting, itching, constipation, ileus, urinary retention, sedation and respiratory depression.

Liposomal bupivacaine has the same active ingredients as bupivacaine. Both act to block the generation and conduction of nerve impulses associated with pain. Liposomal bupivacaine consists of bupivacaine encapsulated within a hydrophobic lipid membrane. Bupivacaine is released from the multivesicular liposomes over a prolonged period of time. [4]

1. Lumber Plexus Blockade Reduces Pain After Hip Arthroscopy: A Prospective Randomized Controlled Trial. YaDeau J, Tedore T, Goytizolo E, Kim D, Green D, Westrick A, Fan R, Rade M, Ranawat A, Coleman S, Kelly B. Anesthesiology & Analgesia 2012; 115(4): 968-972.
2. The analgesic impact of preoperative lumbar plexus blocks for hip arthroscopy. A retrospective review. Schroeder K, Donnelly M, Anderson B, Ford M, Keene J. Hip International 2013; 23(1): 93-8.
3. Are Femoral Nerve Blocks Effective for Early Postoperative Pain Management After Hip Arthroscopy? Ward J, Albert D, Altman R, Goldstein R, Cuff G, Youm T. Arthroscopy: The Journal of Arthroscopic and Related Surgery 2012; 28(8): 1064-69.
4. Liposomal bupivacaine: A long-acting anesthetic for postsurgical analgesia. Formulary 2012.

2.0 Rationale and Specific Aims

Ultrasound guided peri-articular Hip infiltration with local anesthetic solution is an alternative analgesic technique that has been shown to reduce pain, opioid consumption and facilitate earlier discharge from hospital after surgery without causing any weakness of lower extremity. The typical duration of analgesia after peri-articular analgesia lasts only for 8-10 hours. When the effect of injected local anesthetic solution wears off, patients start relying on opioid pain medications for pain control. By using long acting liposomal bupivacaine for LIA we hypothesized that we will provide prolonged duration of analgesia and significantly reduce pain tablet consumption.

3.0 Inclusion/ Exclusion Criteria

Inclusion Criteria:

1. Patients having hip arthroscopy
2. Patients between the ages of 18-80 years

Exclusion Criteria

1. History of neurologic disease, neuropathy, diabetes
2. Allergy to local anesthetic solution
3. Chronic use of narcotics
4. History of previous hip arthroscopy on the ipsilateral side
5. Pregnancy

4.0 Enrollment

Subjects will be consented in a private area prior to surgery. An investigator will explain the study and answer all questions.

5.0 Study Procedures

1. Preoperative evaluation and consent
2. General anesthesia for hip arthroscopy
3. Ultrasound guided injection of liposomal bupivacaine (experimental group) or bupivacaine (control group) (around the anterior, lateral and medial aspect of hip joint.
4. Hip arthroscopy
5. Postoperative recovery – assessment of pain and narcotic consumption using pain scores and 14-question survey
6. Discharge of patients from hospital to home
7. Patient records pain scores and completes 14-question survey
8. Follow up by telephone 24 hours and 96 hours after surgery to collect data

6.0 Reporting of Adverse Events or Unanticipated Problems Involving Risk to Participants or Others

If there are adverse events or unanticipated problems involving risk to the participants or others, they will be reported to the IRB within five working days after their occurrence.

7.0 Study Withdrawal/ Discontinuation

If the participant requests to be withdrawn from the study, the investigator will inform participant that their standard of care will remain the same and that there are no adverse indications from withdrawing. Their withdrawal statement will be added to the participant's Consent Form. The corresponding Study Subject Number will be removed from the study list. Discontinued participant records will not be used to compile the final report.

8.0 Statistical Considerations

Continuous data will be analyzed using parametric methods for normal distribution and non-parametric methods for non-normal distribution (Student t-test or Mann Whitney/Wilcoxon Sum test). Chi-squared or Fisher's exact tests will be used to analyze categorical data. Statistical significance will be set at $\alpha < 0.05$

Sample size of 36 was calculated based on our assumption that a mean difference of 1.0mg (±1 SD) in intravenous hydromorphone administration in the recovery room between the experimental group and control group with a power of 80 % and $\alpha = 0.05$ (2 sided test) and a 10% dropout. Included is the power analysis :

t tests - Means: Difference between two independent means (two groups)
Analysis: A priori: Compute required sample size
Input:
Tail(s) = Two
Effect size d = 1.0
α err prob = 0.05
Power (1-β err prob) = 0.80
Allocation ratio N2/N1 = 1

Output: Noncentrality parameter δ = 2.9154759
Critical t = 2.0369333
Df = 32
Sample size group 1 = 17
Sample size group 2 = 17
Total sample size = 34
Actual power = 0.8070367

9.0 Privacy/ Confidentiality Issues

Patients will be assigned a study subject number that will be used on all data collection documents. Their personal information (Name, address, telephone number, age, weight, height, sex, etc.) will only be recorded on one list with study subject numbers. This list will be separate from all other documents under lock and key and only used to make follow up phone calls. Study records are kept confidential. If the results of the study are published in a scientific journal or presented at a scientific meeting, the subjects' names and any identifiers will not be used.

10.0 Follow-up and Record Retention

The duration of the study will last 96 hours after the participant's total knee replacement. Study records will be stored for three years after the close of the study. Study records will then be destroyed using the standard Saint Francis shredding service.

SAINT FRANCIS HOSPTIAL AND MEDICAL CENTER
Institutional Review Board
Full Board Application for Initial Project Approval

All applications must be typed. Point, click and type in the appropriate cell; cells will expand to accommodate text. Tabbing out of the last cell on the right of a table will insert another row. Referencing the protocol is not acceptable since not all IRB members receive the complete protocol. The IRB reserves the right to return applications that do not provide sufficient responses.

There are consent form templates available for the following study categories, their use is recommended but not required.

Study Categories:

1. For investigational studies involving drug or devices, all sections of this application need to be completed. Use consent template 1.
2. For Full Board social or behavioral research, sections: 1, 2, 3, 4, 5.0-5.3, 6, 7, 8, 9, 10, 11, and 13 need to be completed. Use consent template 2.
3. For establishment of a research registry, sections: 1, 2, 3, 4, 5.0-5.3, 6, 7, 8, 9, 10 and 13 need to be completed. Use consent template 3.

SECTION 1 – BASIC STUDY INFORMATION
1.0 Type of Submission: X INITIAL APPLICATION ☐ RESUBMISSION TO ADDRESS CONTINGENCIES
1.1 Name of Principal Investigator for IRB Proposal: Sanjay K. Sinha
1.2 Project location: X SAINT FRANCIS CAMPUS ☐ BURGDORF CLINIC/BANK OF AMERICA CENTER ☐ MOUNT SINAI CAMPUS ☐ ASYLUM HILL FAMILY MEDICINE ☐ OTHER (PLEASE SPECIFY):
1.3 Type of review requested: X FULL BOARD
1.4 Complete IRB Project Title: Comparison of Bupivacaine to Liposomal Bupivacaine for Ultrasound Guided Peri-articular Hip Infiltration for Postoperative Analgesia after Hip Arthroscopy.
1.5 Complete Associated Grant Title N/A
1.6 Name of PI on the grant: N/A
1.7 Abbreviated Project Title: Ultrasound Guided Local Infiltration Analgesia for Hip Arthroscopy
1.8 Identify any external funding source for this study: N/A
1.9 Identify any internal funding source for this study (e.g. Academic Affairs, dept. funds etc.)**:** Department of Anesthesiology, St. Francis Hospital and Medical Center, Hartford, CT.
1.10 Identify the sponsor for this study (e.g. PI, ECOG, Pfizer, etc)**: N/A**
1.11 Does the PI have any significant financial interest or other relationship with the sponsor? ☐ YES X NO The Research Financial Disclosure Form must be completed by each investigator and submitted with the application.
1.12 Will the PI benefit personally from this study? ☐ YES X NO
1.13 Will the sponsor indemnify subjects in the event of a research-related injury? ☐ YES X NO

Section 2– Research Personnel Information

	Principal Investigator (last, first)	Study Coordinator (last, first if other than PI)	Contact Person (last, first if other than PI or SC)
2.0 Name	Sinha, Sanjay	Patricia Gallo	
2.1 Degree(s) Held	MD	Associates in Science	
2.2 Professional Licenses (type & #)	MD # 035260		
2.3 Professional Certifications	Board Certification in Anesthesiology		
2.4 Job Title	Anesthesiologist	Executive Adm. Assistant To Chief of Staff	
2.5 Department	Anesthesiology	Anesthesiology	
2.6 Mail Code	30301	30301	
2.7 Phone Number	860-714-9666	860-714-9666	
2.8 Emergency Number	860-714-6654	860-830-8629	
2.9 Fax Number	860-714-8110	860-714-8419	
2.10 Pager Number	762-1589		
2.11 E-mail Address	sanjaysinha@comcast.net	pgallo@stfranciscare.org	
2.12 Other Affiliations of PI (e.g. CCMC, Hartford Hospital, Storrs, UCHC)		****************************	****************************

2.13 Off-hours/weekend contact information (Optional):

2.14 Provide a brief summary of the qualifications of the PI to conduct this study and attach an NIH biosketch or complete CV. See attached CV

2.15 Provide information on co-investigators for the study (tabbing out of the bottom right cell will insert another row if needed)

Name (Last, First)	Degrees Held	Licenses (type, St. #) / Certifications	Department	Affiliation	Primary Function(s) Performed In Study
Jonathan Abrams	MD	MD #024924	Anesthesiology	SFHMC	Anesthesiologist, design of study, consent, data analysis
Sivasenthil Arumugam	MD	MD #044509	Anesthesiology	SFHMC	Anesthesiologist, Data analysis
John D'Alessio	MD	MD #030269	Anesthesiology	SFHMC	Anesthesiologist, data analysis
William Suter	Undergraduate student, class of 2016		Summer Research Intern, Department of Anesthesiology		Design of study, data collection, data entry

Additional Information on Co-Investigators (e.g. previous research experience):

Attach an NIH biosketch or complete CV for each co-investigator.

Provide information on research assistants for the study (tabbing out of the bottom right cell will insert another row if needed)

Name (Last, First)	Degrees Held	Licenses (type, St. #) / Certifications	Department	Affiliation	Primary Function(s) Performed In Study

Additional Information on research assistants (e.g. previous research experience):

SECTION 3 – COLLABORATING INSTITUTIONS / MULTI-CENTER TRIALS

3.0 Are there any collaborating sites involved with this study? ☐ YES X NO
(If no skip to 3.3. If yes, proceed to 3.1)

3.1 If collaborating with other sites, provide the name of each institution, and place an x under the column(s) that describes the type of involvement for each institution. Provide the date that the other institution obtained IRB approval or indicate that it is pending.

Institution's Name	Recruitment	Enrollment / Consenting Subjects	Interactions (e.g. survey)	Interventions (e.g. needle stick)	Follow-up	Analysis	IRB Approval Date

Additional Comments:

3.2 Indicate the expected percentage of enrollment at each applicable site, and place an X in the appropriate cell to indicate which institution, based on the preponderance of the expected enrollment, you are requesting serve as the IRB of record or that independent IRB approval will be sought from each applicable site.

Institution's Name	% to be Enrolled/Consented	Requested IRB of Record	Independent IRB Review
SFHMC			

Information on multi-center trials

3.3 Is this a multi-center trial? (If no, skip to section 4, if yes proceed to 3.4) ☐ YES X NO

3.4 Will SFHMC serve as the lead institution? ☐ YES ☐ NO

3.5 Describe the plans for communication among sites in terms of protocol modifications, unanticipated problems and interim results:

SECTION 4 – PROJECT CHARACTERISTICS, SUMMARY AND DESIGN

4.0 Provide the anticipated time frame during which the study will be conducted:

Expected Start Date (mm/dd/yyyy):	Expected Completion Date (mm/dd/yyyy):

06/20/2013	06/20/2014

4.1 Provide the general therapeutic area and sub-area(s) that best describe your study (e.g., cancer, gastrointestinal, pancreatic or psychiatry, addictive behaviors, gambling).

Primary Area	Sub- Area	2nd Sub- Area
Ambulatory Surgery	Recovery Room	

4.2 Place an X after the applicable study phase:

Phase I		Phase II		Phase III		Phase IV (Post Marketing)	X	Not a clinical trial	

4.3 For post-marketing trials, describe any post-marketing requirements imposed on the use of this drug by the FDA. NONE

4.4 Place an X after all characteristics that are applicable to the study design:

Pilot Study		**Case-Control Study**		**Randomization**	**X**
Observational Study		**Double-blind**		**Placebo**	
Cross-Sectional Study		**Chart review**		**Normal Controls**	
Survey		**Focus Group**			
Other (specify): Observer Blinded					

4.5 Provide 2 or 3 sentences describing your project in lay terms. We have previously shown that injecting local anesthetic solution around the hip joint under ultrasound guidance prior to start of surgery will decrease the pain and pain-medication requirements after surgery. This study is being undertaken to compare the pain control using either bupivacaine versus liposomal bupivacaine. Liposomal bupivacaine can potentially provide pain relief lasting up to 72 hours while regular bupivacaine can provide pain relief up to 12 hours.

4.6 Provide a summary description of this project. (Responses 4.7, 4.8 and 4.9 combined should not exceed the equivalent of five pages)

Hypotheses, Objectives and Aims: The objective of this study is to compare the efficacy and duration of infiltration analgesia between liposomal bupivacaine and regular bupivacaine. By using long acting liposomal bupivacaine for LIA we hypothesized that we will provide prolonged duration of analgesia and significantly reduce pain tablet consumption.

Scientific Background and Significance:

Patients undergoing hip arthroscopy experience moderate to severe postoperative pain. Effective pain control after surgery is an important component in the overall management of these patients. Good pain control encourages early participation in rehabilitation program, increases success of the surgery, and improves patient satisfaction. Typically, postoperative analgesia is provided to these patients either with nerve blocks (psoas compartment lumbar plexus block and sciatic nerve block) or opioid medications [1,2,3]. Both these methods provide good pain relief but nerve blocks are associated with weakness of lower extremity muscles which interferes with early ambulation and increase the risk of falls while narcotic medications increase the risk of nausea, vomiting, itching, constipation, ileus, urinary retention, sedation and respiratory depression.

Ultrasound guided peri-articular Hip infiltration with local anesthetic solution is an alternative analgesic technique that has been shown to reduce pain, opioid consumption and facilitate earlier discharge from hospital after surgery without causing any weakness of lower extremity. The typical duration of analgesia after peri-articular analgesia lasts only for 8-10 hours. When the effect of injected local anesthetic solution wears off, patients start relying on opioid pain medications for pain control. By using long acting liposomal bupivacaine for LIA we hypothesized that we will provide prolonged duration of analgesia and significantly reduce pain tablet consumption.

Liposomal bupivacaine has the same active ingredients as bupivacaine. Both act to block the generation and conduction of nerve impulses associated with pain. Liposomal bupivacaine consists of bupivacaine encapsulated within

a hydrophobic lipid membrane. The lipid membrane forms numerous capsules of the drug that are independent of each other (liposomes). Bupivacaine is released from the multivesicular liposomes over a prolonged period of time.[4]

1. Lumber Plexus Blockade Reduces Pain After Hip Arthroscopy: A Prospective Randomized Controlled Trial. YaDeau J, Tedore T, Goytizolo E, Kim D, Green D, Westrick A, Fan R, Rade M, Ranawat A, Coleman S, Kelly B. Anesthesiology & Analgesia 2012; 115(4): 968-972.
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4. Liposomal bupivacaine: A long-acting anesthetic for postsurgical analgesia. Formulary 2012.

Preliminary Studies:

Please attach a copy of the full protocol if available.

4.7 Provide an outline of the experimental design addressing the following: time line of the study from initiation through data analysis, procedures including a time sequence of when those procedures that involve human subjects will be performed and how they will be monitored.

1. Preoperative evaluation and consent
2. General anesthesia for hip arthroscopy
3. Ultrasound guided injection of liposomal bupivacaine (experimental group) or bupivacaine (control group) (around the anterior, lateral and medial aspect of hip joint.
4. Hip arthroscopy
5. Postoperative recovery – assessment of pain and narcotic consumption
6. Discharge of patients from hospital to home
7. Follow up by telephone 24 hours and 96 hours after surgery

Description of sample size:
Two groups of 18 patients each.

Estimated enrollment per year: All subjects will be enrolled in a year

Primary and secondary outcomes and endpoints:
Primary outcome measures will be opioid consumption. Opioid consumption will be recorded intraoperatively (during the surgery), in recovery room and at home after discharge from hospital. Secondary outcome measures will be pain scores (at rest and ambulation) sleep disturbances, constipation, nausea/vomiting and satisfaction with pain management.

4.8 Describe methods of analysis, sample size supported by appropriate power calculations.

Continuous data will be analyzed using parametric methods for normal distribution and non-parametric methods for non-normal distribution (Student t-test or Mann Whitney/Wilcoxon Sum test). Chi-squared or Fisher's exact tests will be used to analyze categorical data. Statistical significance will be set at $\alpha < 0.05$

Sample size of 36 was calculated based on our assumption that a mean difference of 1.0mg (±1 SD) in intravenous hydromorphone administration in the recovery room between the experimental group and control group with a power of 80 % and $\alpha = 0.05$ (2 sided test) and a 10% dropout. Included is the power analysis :

t tests - Means: Difference between two independent means (two groups)
Analysis: A priori: Compute required sample size
Input:
Tail(s) = Two
Effect size d = 1.0
α err prob = 0.05
Power (1-β err prob) = 0.80

Allocation ratio N2/N1 = 1

Output: Noncentrality parameter δ = 2.9154759
Critical t = 2.0369333
Df = 32
Sample size group 1 = 17
Sample size group 2 = 17
Total sample size = 34
Actual power = 0.8070367

4.9 List specific clinical eligibility requirements for subjects, and clinical criteria that would exclude otherwise acceptable subjects.

	Inclusion Criteria	Exclusion Criteria
a.	Patients having Hip Arthroscopy	History of neurologic disease, neuropathy, diabetes
b.	Age 18 – 80 years	Allergy to local anesthetic solution
c.		Chronic use of narcotics
d.		Inability to give consent/cooperate with study
e.		History of previous hip arthroscopy on the ipsilateral side.
		Pregnancy

4.10 Provide the age range or age description of subjects and justification for the age selection:
18 - 80 years

4.11 Are there any non-clinical factors that will exclude subjects, e.g. race/ethnicity, gender, language? If so, justify why the exclusion is necessary. Only English speaking subjects will be included in the study to ensure that the patients understand the protocol, give informed consent and cooperate with the study

SECTION 5 –PROTECTION AGAINST AND MINIMIZATION OF RISKS (45 CFR 46.111(A)(1))

5.0 List all procedures to be performed on human subjects. Also list alternative therapies or procedures that may be advantageous to the subject. Discuss the risks and benefit of any alternative therapy.

Non-Experimental Procedures: Administering oral or intravenous pain medications, Ultrasound guided injection of bupivacaine around hip joint

Experimental Procedures: Ultrasound guided injection of liposomal bupivacaine around the hip joint

Alternative Options: Conventional use of intravenous and oral pain medications ; psoas compartment lumbar plexus block; bupivacaine as locally injected anesthetic

Risks and Benefits of Alternatives:
Benefit: will provide adequate postoperative analgesia
Risk: increased risk of nausea vomiting, sedation, respiratory depression, urinary retention

4.9 Describe the potential risks associated with the proposed research, the procedures to protect against or minimize potential risks and assess the likelihood of the risk occurring and if it were to occur the seriousness to the subject.

Physical Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
-Inadequate analgesia -Systemic local	Vital sign monitoring (Continuous EKG, Blood	Rare	Majority of risks are not permanent in nature

anesthetic toxicity -Infection	pressure, pulse oximetry, capnography) emergency drugs readily available, including Intralipid 20% to treat local anesthetic toxicity, use standard sterile precautions and aseptic injection technique to avoid risk of infection		

Psychological Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
n/a			

Economical Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
None			

Social Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
None			

Legal Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
None			

Other Risks:	Procedures to Protect Against / Minimize Risks	Likelihood of Occurrence	Seriousness to Subject if Risk Occurs
None			

5.2 Describe any costs related to the research activities that are not part of standard of care and indicate who will be responsible for payment, e.g. subject, sponsor, dept. funds.

Research Activity (including medication) Beyond Standard of Care	Party Responsible for Payment
	There will be no additional expense incurred by the patient participating in this study. The patient's insurance carrier will be charged for anesthetic services received as per contract

5.3 Describe any other costs that may be incurred by the subject due to participation in this study, e.g. travel costs, lodging, care for research related injury etc. None

Additional Approvals for Drug Usage Required to Ensure Risks are Minimized and Compliance with IND Regulations

5.4 Will the study involve the use of drugs? (If no skip to 5.11, if yes complete 5.5 – 5.10.) **X YES** ☐ No

5.5 Identify all drugs that will be administered as part of the research study. For studies involving INDs also attach 1) confirmation from the manufacturer of compliance with federal regulations and Good Manufacturing Practices, 2) the 1572 form and 3) if the IND # is not provided, a letter from the sponsor confirming IND approval. When possible submit IND safety reports.

Drug Name	Dosage, Frequency & Duration	Method of Administration	IND # if Available	Manufacturer of IND	Sponsor of IND	Supporting Documents Attached
Liposomal Bupivacaine (Exparel) Experimental Group	*0.4% 60ml solution, once*	*Injection*	*n/a*	*n/a*	*n/a*	*n/a*
Bupivicaine Control Group	*0.25% 60ml solution, once*	*Injection*	*n/a*	*n/a*	*n/a*	*n/a*

5.6 Provide the following information relating to the storage, inventory and dispensing of drugs used in this study. Investigational drugs must be stored in the hospital Pharmacy unless the investigator ensures that storage, dispensing, accountability, and security comply with institutional policy and federal and state laws. The Director of Pharmacy, or delegated pharmacy staff, must approve plans for control of investigational drugs maintained outside of the pharmacy. Investigators who choose to store investigational drugs outside the Pharmacy will be subject to regular auditing by the Pharmacy.

Where will drugs be stored? Anesthesia carts

Describe the storage area and how it meets the required storage conditions for the drug: Anesthesia carts within the Ambulatory Surgery Center

Describe the security measures in place for inventory control and monitoring of the drug inventory: Locked carts

How and by whom will drugs be dispensed? Anesthesiologist performing the procedure

Describe how the disposition of unused drugs will be handled: Unused drugs and syringes are disposed in locked sharps boxes

Drug costs, when applicable, and other Pharmacy expenses associated with the study will be charged to the investigator and must be properly allocated for in the research contract or study budget and reimbursed to the Pharmacy. A department budget or special fund account will need to be provided to the Pharmacy from which the following fees will be drawn: N/A

1. **Study initiation (one time fee)**
2. **Randomization (per subject enrolled)**
3. **Drug preparation and dispensing (per dose)**
4. **Drug cost (for non-sponsored studies)**
5. **Inventory and record keeping (monthly fee which includes quality assurance measures, monitor site visits, and drug storage)**
6. **Study closure (one time fee which includes destruction of remaining drug, copying and archiving study related information)**

***Note that even if the Pharmacy is not storing or dispensing study drugs, study initiation fees will be charged to cover the costs of protocol review and to ensure that drugs not handled by the Pharmacy are in accordance with regulatory standards.**

Additional Information Regarding an Investigational New Drug Application. (If yes to 5.8, 5.9 or 5.10 an IND is needed).

5.7 Has an IND already been obtained for the drug(s) used within the study? (If no, answer 5.8 – 5.10. If yes, be sure information requested in 5.5 is provided and skip to 5.11) ☐ YES X NO

5.8 Is the proposed investigation intended to be reported to the FDA in support of a new indication or to support any other significant change in the labeling for the drug? ☐ YES X NO

5.9 **Is the investigation intended to support a significant change in the advertising for the product?**
☐ YES X NO

5.10 **Does the investigation involve a route of administration or dosage level, or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product?** ☐ YES X NO

Additional Information for Investigational Devices

5.11 **Will the study involve the use of an investigational device?** (If no skip to 5.15, if yes complete 5.12 -5.14)
☐ YES X NO

5.12 **Provide Name, IDE number and manufacturer. For studies involving IDEs also attach confirmation from the manufacturer of compliance with federal regulations and Good Manufacturing Practices and of IDE approval from the sponsor.**

Device Name	IDE Number	Manufacturer of IDE	Sponsor of IDE	Confirmation of GMP Attached	Confirmation of IDE Approval Attached

5.13 **Is the device considered a significant risk or non-significant risk (NSR) device?** ☐ YES ☐ NO
For NSR devices, attach the sponsor's description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of patient selection criteria and monitoring procedures. The sponsor must also inform the IRB if other IRBs have reviewed the proposed study and what determination was made by those IRBs.

5.14 **Describe plans for maintaining inventory of the investigational device.**

Where will the device be stored?
Describe measures in place for inventory control:
Describe measures for monitoring / tracking of the device:
How and by whom will the device be used?
Describe plans for return of unused devices to the sponsor:

Additional Approvals Required from the Institutional Biosafety Committee

5.15 **Does the project involve the use of recombinant DNA?** ☐ YES X NO
If yes provide proof of approval for the study from the Institutional Biosafety Committee. (Approval from the Institutional Biosafety Committee must be obtained prior to seeking IRB approval for all studies that deal with recombinant DNA.)

SECTION 6 –REASONABLENESS OF RISKS IN RELATION TO BENEFITS, IF ANY (45 CFR 46.111(A)(2))

6.0 **Place an X after the level of overall risk that, in the opinion of the PI, is associated with this study.** Comments may also be provided to justify the assessed risk level.

Risk Level	X to select	Comments
None		
Minimal		
Slight Increase Over Minimal	X	
Moderate		
High		

6.1 What benefit, if any, may be gained by the subject and/or society? Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others. Participation in this study will not directly benefit patients, except that the injection of liposomal bupivacaine may provide longer duration of pain control after surgery than the injection of bupivacaine. It will improve our understanding of the efficacy of injecting long acting local anesthetic infiltration analgesia in managing postoperative analgesia in hip arthroscopy patients.

6.2 Discuss the importance of the knowledge that may be gained as a result of the proposed research. Discuss why the risks to subjects are reasonable in relation to the importance of the knowledge that may result. The knowledge gained from this research may provide a method of longer pain control with fewer side effects and earlier mobilization of patients. In the unlikely case that patients receiving local infiltration analgesia may experience more pain, they will be able to receive pain medications without any restriction to keep them comfortable. We expect that both the experimental and control arms of the study will provide better analgesia with fewer side effects when compared to conventional use of narcotic pain medications.

6.3 For studies requiring full board review, describe the scientific review process that the study has undergone. Reviewed by members of Anesthesia Staff

SECTION 7 – SUBJECT SELECTION / RECRUITMENT DATA (45 CFR 46.111(a)(3) &(a)(7)(b))

7.0 Place an x after the type(s) of human subjects that are likely to be recruited for this study. SFHMC does not review/approve research involving prisoners.

Pregnant Women or Fetuses		**Children/Adolescents**		**Inpatients**	
Decisionally Impaired (for non-interventional studies only)		**Viable Neonates**		**Outpatients**	X
SFMHC Employees		**Educationally Disadvantaged**		**Terminally Ill**	
Students, Residents, or Fellows		**Economically Disadvantaged**		**Physically Disabled**	
Other (describe)					

Provide any additional comments to describe subject populations:

7.1 Explain why the inclusion of any vulnerable populations identified in 7.0 is necessary (vulnerable populations include pregnant women or fetuses, neonates, and children): N/A

7.2 What is the maximum number of subjects to be enrolled at SFHMC? 36 subjects

7.3 Explain on what basis it is reasonable to expect that recruitment goals will be met. We perform 100 hip arthroscopies a year at St. Francis Hospital and Medical Center

7.4 If applicable what is the national expectation for enrollment? N/A

Data Collection and Recruitment Methods

7.5 Place an x after the source(s) from which information will be collected.

Medical interventions	X	**Labs results**	X
Existing directly identifiable specimens		**Identifiable Waste material**	
Existing coded specimens		**De-identified Waste material**	
Existing de-identified specimens		**Excess material**	
Interviews	X	**Medical records**	X

Focus groups		Research registry *	

Other sources of information (provide description):

***Provide the name and IRB number of the registry that will be used:**

7.6 Place an X after all methods and materials that will be used to recruit subjects and describe how recruitment strategies will be implemented. (Note: All materials for and methods of recruitment must receive IRB approval prior to use, including final versions of recorded ads for which a script is provided. It is acceptable to identify a recruitment method and note that IRB approval will be sought when the material is developed.)

Methods/Materials	X to Select	Description of Implementation
Radio spots		
Newspapers		
Magazines		
Broadcast messages		
Purchased mailing lists		
Patient base	X	
Flyers		
Phone Calls		
Web postings		

Other methods, materials and strategies that will be used for subject recruitment(provide description):

Describe any outreach programs for recruiting women and minorities into clinical research trials:

*Note: Listing an approved and active clinical trial on the web does not require IRB approval when the posting is limited to the following elements: title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information. IRB review and approval must be sought if any additional information is to be posted. The IRB may conduct random audits of web postings to ensure compliance with these terms.

7.7 Describe any financial or other compensation that will be paid to the subjects and the disbursement schedule for such compensation.
None

SECTION 8 – INFORMED CONSENT PROCESS (45 CFR 46.111(A)(4))

8.0 Have you requested exempt status or a waiver of the requirement to obtain consent ? ☐ YES X NO
(If yes, skip to section 10. If no and study is open to new enrollment, or you have requested exempt status and will be consenting subjects, complete all items in this section.)

8.1 Provide the version reference of consent form submitted for review and approval and submit a completed informed consent checklist.

8.2 Who will be authorized to obtain consent/assent/authorization?

Name of individual(s) authorized:	Fluent in Language(s):
Sanjay Sinha	English
Jonothan Abrams	English

8.3 Are non-English speaking subjects likely to be consented? ☐ YES X NO
If so describe plans for ensuring that information is presented in a language understandable to the subject/Legally Authorized Representative (LAR) If not, explain why. (Translation must be performed by an official translation agency or individual certified to provide translation. Please include translation documentation with the application.)

8.4 Who will provide consent/permission (e.g. the subject, parent, LAR)? Note: LARs can consent only for non-interventional studies. Subject
8.5 If consent will be obtained from LARs, describe the process for ensuring that the LAR is in fact the court-appointed conservator or guardian, or individual designated as having power of attorney for health care, or individuals designated as a health care representative. Consent from next-of-kin is not acceptable absent one of the prior designations. Note: LARs can consent only for non-interventional studies.
8.6 Will anyone other than the subject/LAR be a part of the consent process (e.g. witness)? ☐ YES X NO
8.7 **How will the privacy of the subjects/LARs be maintained throughout the consent process?** The patient will be consented in a private area prior to surgery. Study records and identities will be kept confidential. If the results of the study are published in a scientific journal or presented at a scientific meeting, the subjects names' and identifying information will not be disclosed.
8.8 Describe in detail <u>the process</u> for obtaining consent, including steps that will occur, the estimated length of the discussion, and how will it be ensured that subjects / LARs have had enough time to consider their decision regarding participation. Note: the consenting process needs to be documented in the research record for each subject. During the preoperative evaluation, appropriate subjects will be asked to participate in the study. The procedures, risks, and benefits will be explained by at least one of the investigators.
8.9 How will on-going consent of the subjects /LARs be obtained throughout the conduct of the study? N/A
8.10 Will any screening activity occur prior to consent / authorization being obtained? ☐ YES X NO
8.11 Describe the process of obtaining assent from children or decisionally impaired adults. N/A
8.12 Provide any additional comments regarding the consent process.
Ensuring There Is No Undue Influence Within the Consent Process
8.13 Describe plans to minimize the possibility of coercion or undue influence during the consent process: Patients will be informed that they do not have to participate in the study; they will receive the same standard of care. Patients have the right to withdraw from the study anytime
8.14 What benefit, if any, is to be gained by the research personnel for subject recruitment into the study, e.g. payment for enrollment? If applicable, disclose the value of the benefit and explain how it is justified. None
SECTION 9– INFORMED CONSENT DOCUMENTATION (45 CFR 46.111(A)(5) AND .117(C))
9.0 Will consent be documented via use of a consent form? X YES ☐ NO If a consent document will not be used, a waiver of authorization for disclosure of protected health information must be submitted with the application.
9.1 Would the consent form be the only record linking the subject to the research study? X YES ☐ NO
9.2 Is the principal risk that of potential harm caused if there were a breach of confidentiality? ☐ YES X NO **If yes, describe.**
9.3 Does the research present more than minimal risk? X YES ☐ NO **If no, explain the rationale for this assessment.**
9.4 Does the research involve any procedures for which written consent is normally required outside of the research context? ☐ YES X NO

SECTION 10 - PROTECTION OF PRIVACY OF SUBJECTS & CONFIDENTIALITY OF DATA (45 CFR 46.111(A)(7) & HIPAA)

10.0 How will the privacy interest of subjects be maintained throughout the conduct of the study (note, privacy pertains to the individual not to the data)? Patients will be assigned a study subject number that will be used on all data collection documents. Their personal information (Name, address, telephone number, age, weight, height, sex, etc.) will only be recorded on one list with study subject numbers. This list will be separate from all other documents under lock and key and only used to make follow up phone calls. Study records are kept confidential. If the results of the study are published in a scientific journal or presented at a scientific meeting, the subjects' names and any identifiers will not be used.

10.1 What information, if any, will be sought from the subject about other living individuals? None

10.2 Describe the procedures to protect the confidentiality of data during the conduct of the study by addressing each element noted below (note, confidentiality pertains to the data, not the individual).

Who will own the data (Sponsor, SFHMC or the PI)? SFHMC
Describe plans for storage and security of information on hard copy, including how research records will be labeled and if applicable, how information will be protected during transportation from external sites and from SFHMC. Locked file cabinet in anesthesia office
Will lab results be posted to medical records or research records? Medical records
Will other study related information, e.g. the informed consent document, survey tools, be posted to the medical record or research record? Consent form and survey/data collection form will be placed in research record.
Describe plans for storage and security of identifiable/coded samples. N/A
Describe plans for storage and security of electronic data. Password protected on a SFHMC computer
Describe the security measures that are in place for the equipment that houses identifiable data. Locked file cabinet
Who will have access to hardcopy, samples, and / or electronic data? PI, co-investigators, and coordinator
How will access be managed? Under lock and key
Describe the plans for storage or destruction of identifiable data for screened failures. Locked cabinet

10.3 Describe procedures to continue to protect confidentiality after study closure by addressing each element noted below.

How long will information continue to be stored? 1 year after study is closed, and then information will be archived at Iron Mountain for long-term storage (at least 5 years).
Describe plans for on-going storage and security of hard copy data. Lock and key, password protected
Describe plans for on-going storage and security of identifiable samples. None
Describe plans for on-going storage and security of electronic records. Password protected
Who will have access to hardcopy, samples and/or electronic data? PI, co-investigators, coordinator
How will access be managed? Under lock and key
Describe the plans for the destruction of identifiable data. Shredder

SECTION 11 –SAFETY MONITORING (45 CFR 46.111(A)(6))

11.0 Place an X after the entity responsible for safety monitoring of the study and after the type(s) of safety monitoring in place for this study. For multi-center trials, or trials with external monitoring, submit the monitoring plan; and when applicable the DSMB charter, describing details of membership, frequency of meeting etc., and when possible summaries of DSMB meetings or findings that have already occurred.

Entity responsible for monitoring:		If applicable describe other entities below.
Monitoring internal to SFHMC: Wesley Knauft, MD Woodland Anesthesia 860-714-6654	n/a	
Monitoring by sponsor	n/a	
Monitoring by other entity (describe)	n/a	

Data Safety Plan		**Independent Monitor**	
Data Safety Board		**Other (describe)**	

11.1 Describe plans for communicating significant findings to subjects, in particular those findings that may impact the subject's willingness to continue to participate or that relate to the safety or medical care of the subjects. Subjects will receive a letter if there are any significant findings.

11.2 Provide a brief description of the resources available to conduct this study, including the accessibility/availability of such resources. If a certain type of resource is not needed, explain why.

Resource	Description of available resource	Accessibility /Availability
Financial resources (internal and external)	Department of Anesthesiology	Readily available
Staff (e.g. for medical/professional intervention)	Anesthesiologists, Surgeons, Nurses	Readily available
Equipment (e.g. crash carts, shielding, resuscitation equipment, etc.)	Anesthesia carts, Crash carts, Resuscitation equipment	Readily available
Supplies	OR, PACU supplies	Readily available
Laboratory space	n/a	n/a
Bed space	Hospital	Hospital availability
Services (e.g. counseling, ancillary care)	Hospital based	Hospital availability
Other Resources		
General Comments		

SECTION 12– ADDITIONAL INFORMATION PERTAINING TO GENETIC RESEARCH

12.0 Does the study involve genetic research? ☐ YES X NO

If no skip to section 13. If yes, respond to the remaining questions in this section.

12.1 Will findings related to the study be disclosed to the subject? ☐ YES X NO
(If yes, answer 12.2 – 12.7. If no, skip to 12.8. Note that if the researchers plan to release findings the subjects must also be given the opportunity to decline receiving information.)

12.2 Describe what information will be provided.

12.3 Describe who will provide the information to the subject.

12.4 Describe at what point in the study the information will be provided.

12.5 Describe by what means it will be provided.

12.6 Describe the reliability of information provided.

12.7 Explain the basis upon which the disclosure decision was made.

12.8 Will unexpected and/or unrelated findings be disclosed? Subjects will receive a letter if there are any significant findings

12.9 If findings will be published, explain how the subject's confidentiality will be ensured. The subjects' names and any identifying information will not be used.

SECTION 13 – SIGNATURE OF PRINCIPAL INVESTIGATOR AND DATE

13.0 Indicate if this protocol, or one similar to it, has previously been denied approval by any IRB panel. If it has previously been denied approval, also provide details regarding the IRB that denied approval, for what reasons approval was denied, when it was denied and how the concerns have been addressed.

13.1 Signature of Principal Investigator. The undersigned assures that all key study personnel 1) have completed the required human subjects training, 2) are knowledgeable of the protocol and the institutions policy for reporting unanticipated problems, non-compliance (protocol deviations/violations) and adverse events, 3) commit to conducting the study in accordance with the protocol as approved by the IRB, state law, federal regulations, SFHMC policies and with the ethical principles of respect for persons, beneficence and justice as set forth in the Belmont Report. The undersigned also accepts primary responsibility for all aspects of the management of this study.

Signature.....

Date.....06/10/13.....