Study Protocol & Procedures:
Local Anesthetic / Post-operative Pain Trial
IRB #: 008-197

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Protocol

[1]**Background:** Patients receiving a new pacemaker or defibrillator are currently given Bupivacaine, Lidocaine, or a mixture of the two for local anesthetic treatment (in addition to general anesthesia). The choice of local anesthetic to be used during surgery is based primarily on the differences in time for the anesthetic to take effect and duration thereafter. Lidocaine typically works in less than 1 minute and lasts approximately 45 minutes. Bupivacaine works within 2 to 3 minutes and lasts 4 to 6 hours. Lidocaine is often preferable due to its shorter time of effectiveness. However, its relatively short duration may translate into a higher use of intravenous (IV) narcotics for pain management during postoperative care – particularly within the first hour following emergence from general anesthesia. Therefore it is conceivable that these patients would have higher levels of pain as well as higher cost of care related to cost of narcotics and caregiver time required to administer them.

[2]**Objectives:** The goal of the proposed study is to investigate the relationships between treatment with lidocaine or a mixture of lidocaine and Bupivacaine and pain, consequent narcotic treatment, and patient movement during anesthesia while adjusting for other clinical and/or demographic factors in consecutive subjects who undergo arrhythmia surgery at Baylor Heart and Vascular Institute over several months.

[3]This study will focus primarily on assessing the relationship between local anesthetic choice and postoperative pain for patients who receive a new pacemaker or defibrillator. The primary outcome of interest is: pain as measured by a standardized and validated scale, the Visual Analog Scale (VAS) at 3 time points: prior to surgery, once awakened from surgery, 4 hours after, and 4-24 hours after. The secondary outcomes of interest are: IV narcotic use (including dosages and strength of narcotic) within 1 hour after the patient emerges from general anesthesia and patient movement during the insertion of pacemaker or defibrillator. Data source: All data for the proposed investigation will be abstracted from the patient charts included in the study cohort.

[4]**Study Design:** The proposed investigation is a randomized trial comparing the efficacy of two standard local anesthetic treatments in terms of postoperative pain and narcotic use following pacemaker or defibrillator insertion. Standard local anesthetic choice will be classified as Lidocaine (a standardized dose of 10 cc 1% solution) or a combination of Bupivacaine and Lidocaine (a standardized dose of 6 cc 1% Lidocaine mixed with 4 cc 0.25% Bupivacaine solution). Both solutions are clear with a total volume of 10 cc. The BHVH pharmacy will draw up the appropriate treatment, rendering the surgeon administering the local anesthetic blinded to the identity of the local anesthetic. Volume administered as well as other clinical and demographic data will be obtained for each patient. Pain will be measured using the VAS (a standardized and validated scale) at 3 time points: prior to surgery, once awakened from surgery, 4 hours after, and 4-24 hours after. The type, number, and dose of narcotics will be collected up to 24 hours after patient awakens from surgery. The study cohort will comprise all consenting patients who undergo new pacemaker or defibrillator insertion and consent to have data collected regarding the insertion of a pacemaker/defibrillator device at Baylor Heart and Vascular

(Dallas, TX) between 11/03/2008 and 08/30/2012, approximately 350 patients. Additional Study Procedures are attached after the protocol.

[5]**Inclusion Criteria**: Patients consenting to routine data collection in Apollo at Baylor Jack and Jane Hamilton Heart and Vascular Hospital, at least 18 years of age, and receiving only: ICD implant, single chambered pacemaker implant, or dual chambered pacemaker implant, for whom either Lidocaine or Bupivacaine is not contraindicated.

[6]**Exclusion Criteria:** Patients not consenting to routine data collection in Apollo at Baylor Jack and Jane Hamilton Heart and Vascular Hospital; and/or under 18 years of age; and/or receiving procedures other than: ICD implant, single chambered pacemaker implant, or dual chambered pacemaker implant; and/or Lidocaine or Bupivacaine is contraindicated.

[7]**Risks:** Risks incurred as a result of administering lidocaine or lidocaine / Bupivacaine mixtures for this study will be no different than the risks incurred via administration of either treatment as a result of standard care in pacemaker / defibrillator insertion. These risks include: CNS depression, CNS excitement, cardiac arrhythmias, allergic reaction, and trouble breathing (allergic reaction, low blood pressure, difficulty breathing, fast heart rate, slow heart rate, feeling light headed, tremors, seizure, chest pain, weak pulse, nausea, vomiting, anxiety, speech problems and headache).

[8]**Potential Benefits:** It is possible that one treatment may result in diminished pain post-surgery. This would result in diminished pain for those participants assigned to that specific treatment group. This research may benefit individuals in society by revealing a more cost effective treatment with less pain incurred after implementation of pacemaker/defibrillator devices.

[9]**Risk to Benefit Analysis:** Patients receiving a pacemaker or defibrillator are currently given Bupivacaine, Lidocaine, or a mixture of the two for local anesthetic treatment (in addition to general anesthesia). The choice of local anesthetic to be used during surgery is based primarily on the differences in time for the anesthetic to take effect and duration thereafter. Lidocaine typically works in less than 1 minute and lasts approximately 45 minutes. Bupivacaine works within 2 to 3 minutes and lasts 4 to 6 hours. Lidocaine is often preferable due to its shorter time of effectiveness. However, its relatively short duration may translate into a higher use of narcotics for pain management during postoperative care – particularly within the first hour following emergence from general anesthesia. Therefore it is conceivable that these patients would have higher levels of pain, higher cost of care related to cost of narcotics, and higher cost of caregiver time required to administer them. Either treatment is standard for these procedures, so no additional risk will be incurred by assigning treatment to either Lidocaine or Bupivacaine/Lidocaine mixture.

[10]**Payment/ Compensation/ Subject Costs:** The research subjects will not receive a stipend for participation in the study. There will be no cost to the subjects.

Confidentiality

[11]**Data Storage:** An appropriate database will be created and managed in compliance with HIPAA regulations. Data will be stored safely in a secure environment, and maintenance for back-up purposes will be performed on a routine basis.

[12]**Research Subject Privacy:** Patients will be approached discretely and privately by the study coordinator on location at Baylor Heart and Vascular Hospital prior to their procedure. The discretion of the study coordinator will be used to judge if privacy (from both medical personnel and other persons in the hospital) is ensured during the consent process. The patient will be informed that they can stop the consent process at anytime if they feel their privacy is being compromised. No information will be collected directly from the patient after this point. Patient will be informed that participating / not participating in this study will in no way affect their care and that they are in no way obligated or expected to participate. If the patient agrees to participate, they will be taken through the informed consent process. Upon data acquisition, study identifiers will be encrypted to protect patients' privacy and meet HIPAA regulations, and data will be stored in a secured database while periodic back-up will protect against catastrophic data loss. All hard copy material (summary printouts) will be stored by the principal investigator in locked file cabinets and the disks, diskettes, and other removable storage media files will be safely stored as per HIPAA regulations. The ability to decode the study identifier will be restricted to the principal investigator.

Study Procedures:

Defining potential participants
Timing: **1 day prior to surgery:**

On-Site Study Coordinator:

- On-Site Study Coordinator will access the EP's schedules via MediTech one day prior to surgery. Those patients receiving any of the following may be considered for inclusion in the study:
    - BiVD (CRT)
    - ICD
    - Pacemaker
- On-Site Study Coordinator will contact Electrophysiologist to gain permission to approach patient.

WebEx Login info:
Web address: http://sphinxanesthesia.webexone.com
Login Name:
Login Password:

Consent and Randomization
Timing: **Day of surgery – Prior to procedure immediately following consent.**
Location: **4th Floor BHVH.**

On-Site Study Coordinator:

- On-Site Study Coordinator will approach patient the day of procedure, *prior to procedure* in patient room to consent patient.

- On-Site Study Coordinator will retain a signed copy of the consent document. The study participant will also be provided a copy of the consent document.

- On-Site Study Coordinator will determine randomization assignment of each participant the day of procedure after having consented the participant. Randomization will occur as follows:

    - Within the randomization notebook, the section corresponding to the appropriate EP will be selected.
    - Within this section, the appropriate procedure subsection (based upon the gender of the participant) will be selected.
    - Within this section, the subsection representing the patient's procedure type will be selected.
    - In first available slot on the procedure type section, the On-Site Study Coordinator will enter the patient's name, MRN and social security number in the appropriate location.
        - Treatment assignment number will be listed to the right of SSN.
        - The treatment assignment number correlates to an envelope with the treatment assignment sealed within to be brought to the BHVH pharmacy, **only to be opened by the pharmacy staff.**

- On-Site Study Coordinator will attach a study participation letter onto the patient's chart prior to EP entry into the surgical room.

On-Site Study Coordinator will inform nursing staff of patient enrollment into study **(on 3rd floor BHVH)**.

Treatment Preparation
Timing: **Day of surgery – Prior to EP entering EP suite.**
Location: **3rd Floor BHVH**

EP nursing staff:

- EP nursing staff will look at patient chart to identify if study participation letter is present and notify the electrophysiologist.

- EP nursing staff will provide the electrophysiologist with the pre-drawn syringe.

- EP nurse will report "local anesthetic" and dosage in the patient's chart as per usual procedure.

Surgical Procedure
Timing: **Day of surgery - During surgical procedure / device implantation**
Location: **3rd floor BHVH**

EP Nursing staff:

- Please follow standard protocol for recording/measuring pre-operative pain.

Anesthesiologist:

- You will have no real responsibilities for this trial; however, we do ask that you **standardize the anesthesia protocol with fentanyl and propofol** (using anything else such as midazolam, sufentanyl, etomidate, pentothal, ketorolac and local anesthetics like mepivacaine could disqualify the patient).

- Dosing should be based on individual patient factors and your judgment.

- **If for any reason you must deviate from this protocol, please notify On-Site Study Coordinator and/or research coordinator.**

Surgeon:

- You will administer local anesthetic as given to you by the EP nursing staff.

- If for any reason you are required to give more local anesthetic, you may do so, but it is important that the supplemental administration be documented in the Apollo report.

- **Please notify On-Site Study Coordinator or research coordinator if you are required to administer more local anesthetic.**

Data abstraction and adverse event monitoring
Timing: Post-surgery

EP Nursing Staff:

- Please follow standard protocol for recording/measuring post-operative pain.

On-Site Study Coordinator:

- On-Site Study Coordinator will check EP lab records to determine local anesthetic given to patient.
- On-Site Study Coordinator will abstract chart information onto case report form.
- Adverse events will be determined from patient charts and reported within 7 days.
- All forms will be forwarded to the research coordinator.

Treatment verification and continued monitoring
Timing: **Post-surgery (daily):**

Research coordinator:

- Research coordinator will verify randomization number received correct study medication.

- BHVH data will be queried to verify all patients are discharged post-surgery (disposition type, disposition date, and discharge date will be queried). If they are not discharged this may constitute serious adverse event (SAE) and research nurse or coordinator will report to IRB immediately (within 24 hours).