Efficacy of Liposomal Bupivacaine for Prolonged Postoperative Analgesia in Patient Undergoing Breast Reconstruction with Tissue Expander

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PACIRA Pharmaceuticals, Inc

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I. APPLICATION INFORMATION

- Principal Investigator: Raymond Isakov, MD/ Staff & Associate Program Director
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II. SUMMARY OF GRANT REQUEST

- Title of Proposed Project:

Efficacy of liposomal bupivacaine for Prolonged Postoperative Analgesia in Patient Undergoing Breast Reconstruction with Tissue Expander: Assess best technique for infiltration of liposomal bupivacaine and evaluate the effectiveness of DepoFoam Bupivicaine (Exparel®) to reduce postoperative pain in breast reconstruction patients compared to the current standard treatment (bupivacaine HCl).

- Study Coordinator:

  Rafael A. Couto, MD/ Resident: Plastic Surgery/ CCF

- Institution/Organization:

  Plastic Surgery & Dermatology Institute/ Cleveland Clinic Foundation Main Campus

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- Co-Investigators:

1) Steven Bernard, MD/ Staff & Program Director: Plastic Surgery CCF
2) Andrea Moreira, MD/ Staff: Plastic Surgery/ CCF
3) Risal Djohan, MD/ Staff: Plastic Surgery/ CCF
4) Graham Schwarz, MD/ Staff: Plastic Surgery/ CCF
5) Randal Yetman, MD/Staff: Plastic Surgery/ CCF
6) Rafael A. Couto, MD/ Resident: Plastic Surgery/CCF
7) Paul Durand, MD/ Resident: Plastic Surgery/ CCF
8) Steven Rueda, MD/ Resident: Plastic Surgery/ CCF
9) Jason Korn, MD/ Fellow: Plastic Surgery/ CCF

- Product Support Requested from Pacira (description, dosage & quantity):

  Description: Exparel® (liposomal bupivacaine)

  Dosage: 266 mg

  Quantity: Because we are planning to use 266mg, the final amount of units (266mg) of Exparel that will be requested will depend on number of unilateral and bilateral breast reconstruction included in the study. Therefore, the number of units requested will range from 25 – 60 units.

- Are you requesting Pacira to be the sole supporter of this study?

  Yes

- Please specify additional sources of support (if applicable)

  Not applicable

III. STUDY INFORMATION

- **Study Design Abstract**

Study rationale:

Control of postoperative analgesia has become a major topic in surgical awareness and it plays a crucial role in patient satisfaction and outcome.[1,2] Breast reconstruction is associated with postoperative pain, which can result in patient discomfort, patient dissatisfaction, and unanticipated/extended hospital admission when undermanaged.[2-4] Opioids continue to play an important role in postoperative pain management.[5] However, their use concerns patients and physicians, since their side effects (e.g. nausea/vomiting, pruritus, sedation, respiratory/cardiovascular depression) can become detrimental to patient recovery. [2,5]

Long lasting local anesthetics (bupivicaine HCl) have become a useful tool to reduce postoperative pain and cumulative narcotics usage in breast reconstruction patients.[2-4] However, because bupivacaine HCl is only effective for a brief period of time (3-7 hours)[6], postoperative pain control is then mostly achieved by intermittently administrating bupivacaine HCl through an indwelling catheter (ON Q pump) into the surgical site.[2-4] This therapeutic modality has several disadvantages: 1) patients must leave hospital with the device; 2) catheter can become dislodged; 3) seroma formation can occur; and 4) potential infections through the introduction of skin flora into a sterile pocket.[7,8] In contrast to bupivicaine HCl, liposomal bupivacaine; Exparel®; Pacira Pharmaceuticals, San Diego, CA) has demonstrated a decrease in the use of rescue opioid analgesics and longer lasting postoperative pain control.[9-11] Therefore, in the breast reconstruction patient population, liposomal bupivacaine long-lasting effect not only allows us to treat postoperative pain without the need of a local anesthetic infusion pump, but also reduce postoperative opioid use.

We believe that subjects undergoing breast reconstruction with tissue expander will achieve greater control of pain and longer lasting analgesia with the use of liposomal bupivacaine compared to bupivicaine HCl. Consequently, the group managed with liposomal bupivacaine will have less of a need for rescue analgesic medications, fewer narcotic adverse events (e.g. nausea/vomiting), and shorter hospital stays than subjects treated with bupivacaine HCl. We strongly believe that this study will be of great interest to the plastic and reconstructive surgery

community, because it can significantly influence what may soon be considered 'standard of care' in this patient population.

Objectives/Rationale/Hypothesis

Objective 1:

Evaluate the effectiveness of DepoFoam Bupivicaine (Exparel®) to reduce postoperative pain in breast reconstruction patients compared to the current standard treatment (bupivacaine HCl).

We will assess pain utilizing methods that have been successfully employed in studies with similar experimental design.[9-13] Pain will be assessed qualitatively through the use of: 1) numeric rating scale during rest (NRS-R) and activity (NRS-A), 2) brief pain inventory (BPI) questionnaire, and 3) postoperative analgesia patient satisfaction scale.

The numeric rating scale of pain (NRS) will consist of an 11 point scale. The end points are extremes of pain: no pain (NRS=0) and worst possible pain (NRS=10) (Appendix 1, Figure 1). We will also utilize the brief pain inventory (BPI) questionnaire to assess the patient's quality of life after surgery (Appendix 2). The BPI measures both the intensity of pain (sensory dimension) and interference of pain in the patient's life. This questionnaire assesses pain relief, pain quality, and patient perception of the cause of pain (Appendix 2).[14] Furthermore, postoperative analgesia satisfaction will be recorded through a 5-point scale (0= very unsatisfied to 5= very satisfied) (Appendix 1, Figure 2).

Rationale:

There is no current literature evaluating the effectiveness of DepoFoam Bupivicaine (Exparel®) in reducing postoperative pain in breast reconstruction patients compared to the current standard treatment (bupivacaine HCl).

Hypothesis:

We hypothesize that patients undergoing breast reconstruction with tissue expander will achieve greater control of post-operative pain and longer lasting analgesia with the use of liposomal bupivacaine.

Objective 2:

Evaluate and compare the usage of opiate rescue pain medications between the experimental (liposomal bupivacaine) and historical control (bupivacaine HCl) groups.

Given the subjective nature behind pain assessment, we will record the use of rescue analgesics for each patient. This part of the study will provide quantitative data that we can then use in comparison to the qualitative measurements (NSR, BPI, patient satisfaction scale rate). In turn, this will allow us to objectify patient's pain, thereby increasing the validity of our results. More importantly, this aspect of the investigation will enable us to study the impact that liposomal bupivacaine has in reducing the postoperative usage of opioid medications in this patient population.

Rationale:

There are no studies evaluating the effectiveness of liposomal bupivacaine in reducing the usage of opioid analgesics in breast reconstruction patients compared to the current standard treatment (bupivacaine HCl).

Hypothesis:

Patients managed with liposomal bupivacaine will have a reduced need for opioid medication management compared to subjects treated with bupivacaine HCl.

Design of Study:

The pilot study will be a prospective.

Inclusion Criteria

All eligible patients, 18 and over, undergo breast reconstruction with tissue expanders.

Exclusion Criteria

Exclusion criteria include the following patient populations: 1) history of adverse reaction to local anesthesia; 2) chronic liver disease; 3) history of chronic preoperative consumption of narcotics or opioids; 4) history of alcohol and/or illicit drug dependence; 5) undergoing

combined procedures; 6) diagnosed with neuromuscular/neurosensory disorder; 7) positive pregnancy test; 8) previous breast conservation therapy (lumpectomy with radiation treatment; 9) previous surgeries or trauma in the breast or chest region (denervation may bias pain perception); 10) axillary node dissection; and 11) psychosis.

Screening Visit

Screening procedure will be performed within 30 days of the patient's scheduled procedure. During screening visit: 1) informed consent will be obtained; 2) study eligibility will be confirmed; 3) evaluation will be performed (i.e. medical/surgical history, physical exam, vital signs, drug/alcohol screening, and clinical laboratory); and 4) patient will be trained on the pain assessment tools that will be used in the study.

Preoperative

Preoperative evaluation will be performed prior to the operation (e.g. eligibility reconfirmation, review of history, vital signs, physical exam, urine pregnancy test). Furthermore, patient's baseline pain intensity will be assessed at this time. Pain intensity at both rest and with activity will be assessed using the numeric rating scale (NRS-R & NRS-A; 0= no pain & 10= worst possible pain, respectively). When assessing NRS-A pain intensity, we will ask the patient to raise both arms above the head and hold for five seconds. Patient will be randomly assigned to either receive Depofoam bupivacaine (266mg per side) or bupivacaine HCl (2.5mg/kg) in a 1:1 ratio. Randomization and allocation of the subjects chosen to be placed into the experimental group (DepoFoam bupivacaine) or control group (bupivicaine HCl) will be generated via a computer randomization system. (Note: A standard final dilution of the drugs will be established among the co-investigators prior to initiating the study).

Intraoperative

General Anesthesia Protocol:

All eligible patients will receive the same anesthetic plan to minimize the incidence of postoperative nausea and vomiting:

1. Premedication with midazolam
2. Administration of decadron at induction to prevent nausea and vomiting

3. Induction with propofol and alfentanyl, muscle relaxation with succinycholine, rocuronium or atracurium
4. Anesthesia maintenance with propofol, alfentanyl, nitrous oxide, and oxygen
5. Anesthesia reversal with neostigmine and glycopyrolate
6. Dolasentron to be given within 30 minutes of emergence

Local Anesthetics Protocol: (Depofoam bupivacaine & Bupivicaine HCl)

The study drugs will be administered into the right and/or left breast of each patient 30 minutes prior to the creation of the subpectoral muscle pocket (where tissue expanders will be placed).

The local anesthetic will be administered using a "field block" approach. The patient will be in supine position, with each arm abducted at the shoulder and placed on an arm board. We will administer the drug with a 10 or 20 ml syringe and 22- or 25-gauge. The local anesthetic will be locally infiltrated into the pocket (where implants are placed) and around the perimeter of the surgical site, including the drain sites. We will be infiltrating the drugs to soft tissue, chest wall and muscles. Because several surgeons will be involved in this study, we will develop a standardized protocol for administering the local anesthetic; not only this will reduce any potential confounding factors, but also will enable us to be consistent. Patients from surgeons that are not part of the study may be enrolled as long as the surgeon is familiarized with the protocol, agrees with it, and one of the co-investigators is present during the research related procedures to assure compliance.

Postoperative

Pain Assessment

We will assess pain utilizing methods that have been successfully employed in studies with similar experimental design.[9-13] Subjective evaluation of pain will be recorded on a Patient Data Collection Sheet. It will be performed by using numeric rating scale (Appendix 1; Table 1, Figure 1). Pain intensity at rest and with activity will be assessed using the numeric rating scale (NRS-R & NRS-A; 0= no pain & 10=worst possible pain, respectively). When assessing NRS-A pain intensity, we will ask the patient to raise both arms above the head and hold for five seconds. NRS-R and NRS-A pain intensity assessment will be recorded at one, four, eight, 12, 24, 36, 48, 60, 72, 84, and 96 hour time periods after the administration of the local anesthetic. Also patient's quality of life will be assessed by asking her to complete the Brief Pain

Inventory (BPI) questionnaire at 24, 48, 72, and 96 hours (Appendix 2). Furthermore, patient postoperative analgesia satisfaction will also be rated through the use of a 5-point categorical scale (0=very unsatisfied and 5=very satisfied) at 96 hours after local anesthetic administration (Appendix 1, Table 4).

Objective evaluation of pain will be accomplished by assessing the amount and type of rescue analgesics used during hospitalization and post-operative days 1 through 4. This will be evaluated through nursing records available in our electronic medical record (EPIC; Verona, Wisconsin) that will be transferred to a Patient Data Collection Sheet (Appendix 1). During the hospitalization, for postoperative rescue analgesics, patients will have the following available: 1) acetaminophen 650mg (Tylenol) every 4-6 hours as needed for mild pain (pain scale 1-3), 2) oxycodone 5mg/ acetaminophen 325 mg (Percocet) or hydrocodone 5 mg/ acetaminophen 300 mg (Norco) every 4-6 hours as needed, for moderate pain (pain scale 4-6), and 3) IV opioid analgesics (e.g. Dilaudid, Fentanyl, or Morphine) every 4-6 hours as needed, for severe pain (pain scale 7-10). Patient will be discharged with a standardized oral pain medication regimen, which will consists of 1) acetaminophen 650mg and 2) oxycodone 5mg/acetaminophen 325 mg (Percocet) or hydrocodone 5 mg/ acetaminophen 300 mg every 4-6 hours as needed.

Typically, patients undergoing this procedure are discharged from the hospital once tolerating oral pain medications, and no longer requiring IV rescue analgesics. Patients that are getting discharged will receive a similar Patient Data Collection Sheet used during their hospitalization to record their pain, use of rescue analgesics, and adverse events at the remaining time points. For example, if patient is discharged after 24 hours, we will have already assessed and recorded patient's data as explained above at 1, 4, 8, 12, and 24 hour intervals. Then, we will ask the patient to record at home for the remaining intervals: 1) NRS-A and NRS-R at 36, 48, 60, 72, 84, and 96 hours after drug administration; 2) rescue analgesics intake at 36, 48, 60, 72, 84, and 96 hours after drug administration; 3) adverse events at 36, 48, 60, 72, 84, and 96 hours after drug administration; 3) BPI at 24, 48, 72, and 96 hours after drug administration; and 4) 5-point categorical scale at 96 hours (Appendix 1, 2). Patients will be seen at the Plastic Surgery office for their postoperative visit, usually within 7 to 14 days after surgery.

Adverse Events:

The following adverse events will be evaluated: 1) nausea; 2) vomiting; 3) constipation; 4) somnolence; 5) dizziness; 6) respiratory distress. They will be assessed at 1, 4, 8, 12, 24, 36,

48, 60, 72, 84, and 96 hours after the administration of the local anesthetics and recorded in the Patient Data Collection Sheet (Appendix 1, Table 3).

Summary of Methods:

Historical Comparator/Control

The comparator/control of the study will be bupivicaine HCl (Marcaine 0.5% with epinephrine 1:200,000). We are interested in utilizing bupivicaine HCl as the control because: 1) it has been shown to reduce pain scores and cumulative pain medications in breast reconstruction patients[2-4] and 2) the use of local anesthesia for reduction of postoperative analgesia following a breast reconstruction with tissue expander is a standard of treatment at our institution.

Secondary Endpoints

The secondary endpoints of this study will be: 1) adverse events (i.e. nausea/vomiting, somnolence, dizziness, constipation, respiratory distress); 2) overall patient satisfaction; 3) length of hospital stay.

Predictive Variables:

The predictive variables will include: 1) demographics (e.g. age, race/ethnicity, weight/BMI); 2) unilateral/bilateral breast reconstruction; 3) sentinel lymph node biopsy; 4) therapeutic/prophylactic mastectomy; 5) use of acellular dermal matrix (ADM) for reconstruction of the lateral & inferior mammary fold (partial submuscular pocket with ADM); 6) elevation of the serratus anterior (complete submuscular pocket); 7) volume of saline in the tissue expander.

Expected Results

We hypothesize that patients undergoing breast reconstruction with tissue expander will achieve greater control of post-operative pain and longer lasting analgesia with the use of DepoFoam bupivacaine compared to bupivicaine HCl. Consequently, patients managed with DepoFoam bupivacaine will have lower use of opioid rescue medication, fewer narcotic adverse events, and shorter hospital stay than subjects treated with bupivacaine HCl.

Outcome Assessment

Statistical analysis will be conducted on Stata 11.0 (College Station, TX). Patients will be randomly divided into an experimental and control group. Primary and secondary outcomes will be recorded.

Patient population demographics in the two groups will be compared by Fisher's exact test for nominal variables and Student t-test for quantitative variables. This will ensure that conclusions are not due to varying patient populations. Univariate analysis comparing primary outcome measures for both groups will be performed using Mann-Whitney test given expected non-normal distribution of values. The same will be done for secondary end points. Finally, exploratory multivariable regression analyses for each primary end point will be performed to control for the effect of differences in baseline variables between treatment groups on primary endpoint outcomes and avoid erroneous conclusions due to confounding; this will also enable us to evaluate if use of DepoFoam bupivicaine was an independent predictor of the primary and secondary outcomes of this study. Continuous measures will be compared using linear regression techniques, while, if feasible, categorical outcomes will be evaluated using generalized linear models including logistic regression and Poisson regression as appropriate. If necessary, transformations of outcome measures will be performed prior to analysis to meet model assumptions. Analyses will be performed assuming a 0.05 significance level.

- Therapeutics to Be Studied:

  1) Liposomal bupivacaine [bupivacaine extended-release liposome injection, (Exparel®)]
  2) Bupivicaine HCl (Marcaine)

- Pathology and Disease to be Studied and Incidence:
  No disease or pathology will be studied or treated in this investigation. We will be studying the effectiveness of local anesthetics (liposomal bupivacaine & bupivacaine HCl) in post-operative analgesia, following bilateral breast reconstruction with tissue expander.

- Number of Study Subjects/Animals:
  As this is a pilot study, a sample size of 50 total patients (25 per treatment group) is planned. The goal is to have 25 completed patients in each group. Patients that for some reason did not complete the post-operative pain assessment will be replaced. This sample size should

provide estimates of potential effect sizes and variability in the present setting to allow for future study planning. In keeping with recommendations from Cocks et al[15], if the variability is similar to what was observed in Smoot et al[10], then this study should provide adequate evidence of whether pain decreases of 15% or more are unlikely in this setting.

- Dosage Regimen:

Local Anesthetics:

1) Liposomal bupivacaine: 266mg per side (Note: A standard final dilution of the drugs will be established among the co-investigators prior to initiating the study).
2) Bupivicaine HCl: 2.5 mg/kg

Postoperative Pain Rescue Medications During Hospitalization:

1) Acetaminophen 650mg (Tylenol) for mild pain (pain scale 1-3).
2) Oxycodone 5mg/acetaminophen 325mg (Percocet) or hydrocodone 5mg/acetaminophen 300 mg (Norco) 4-6 hours as needed for moderate pain (pain scale 4-6).
3) IV opioid analgesics (e.g. Dilaudid, Fentanyl, or Morphine) for severe pain (pain 7-10).

Pain Medications After Discharge:

1) Acetaminophen 650mg every 6 hours as needed.
2) Oxycodone 5mg/acetaminophen 325 mg (Percocet) or hydrocodone 5 mg/ acetaminophen 300 mg (Norco) 4-6 hours as needed.

- Will IRB and/or Ethics Board Approval be Obtained?

Yes

- Anticipated Date for Review and Approval

April 2013

- Will Informed Consent be Obtained from All Study Subjects

Yes

- Please Describe Your Process for Obtaining Informed Consent and Anticipated Timeline:

For this investigation, patients will be interviewed at the CCF Plastic Surgery Clinic in a private office. Full explanation about the research will be provided. The patient will have the option to participate in the study, not participate, or decide at a later time. If a subject

decides to participate in the study, a written consent document that includes all of the elements of this study will be provided to the patient. Her signature will be obtained on this consent. She will be consented by the PI or co-investigators only. If she decides to participate at a later time, we will discuss the study one more time before the surgery. This meeting will be documented in the patient's electronic medical record (EPIC software) as an office encounter and signed by the person obtaining the consent.

- Do you have a Plan for Documenting/Reporting Adverse Events?
  Yes

- Please Describe Plan for Documenting/Reporting Adverse Events
  The following adverse events will be evaluated: 1) nausea; 2) vomiting; 3) constipation; 4) somnolence; 5) dizziness; 6) respiratory distress. They will be assessed at 1, 4, 8, 12, 24, 36, 48, 60, 72, 84, and 96 hours after the administration of the local anesthetics and recorded in the Patient Data Collection Sheet (Appendix 1, Table 3).

- Study Duration
  We estimate that the study will take approximately 6 months.

- Anticipated Start Date:
  We estimate to start the investigation in May 2014

- Anticipated Finish Date:
  We estimate to finish the study by November of 2014

IV. PUBLICATION

- Do you plan on registering this study on a public database?: No
- Publication/Presentation Plan:

  Peer-Reviewed Journals: 1) Plastic & Reconstructive Surgery
  2) Annals of Plastic Surgery

  Meetings: 1) American Association of Plastic Surgeons (AAPS) Annual Meeting
  2) American Society of Plastic Surgeons (ASPS) Annual Meeting
  3) The Ohio Valley Society of Plastic Surgeons (OVSPS) Annual Meeting
  4) Plastic Surgery Research Council (PSRC) Annual Meeting

V. OTHER PACIRA SUPPORT REQUESTED

Description: Exparel® (Depo Foam bupivacaine)

Dosage: 266 mg

Quantity: Because we are planning to use 266mg per side, the final amount of units (266mg) of Exparel that will be requested will depend on number of unilateral and bilateral breast reconstruction included in the study. Therefore, the number of units requested will range from 25 – 60 units.

VI. APPENDIX

Please see next page

Appendix 1- Patient Data Collection Sheet

Name:
Subject Number:

Patient Data Collection Sheet

Day 1:

Table 1: Numeric Pain Rating Scale

Instructions: Please record the number that best describes the level of pain (Figure 1) during rest and activity (raise both arms above the head and hold for five seconds) on the respective time points.

Time Points	Numeric Pain Scale (Rest)	Numeric Pain Scale (Activity)
1 hour		
4 hours		
8 hours		
12 hours		
24 hours		

Figure 1: Numeric Pain Rating Scale

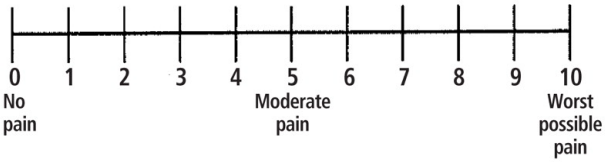


Table 2: Pain Medications

Instructions: Please record the amount & frequency of each medication that you have taken on the respective time points. Only include medications that were taken, since the last time point. Do not include medications already included in previous time points (even if they overlap).

Time Points	Tylenol (Amt/Dose/ Freq)	Percocet (Amt/Dose/ Freq)	Norco (Amt/Dose/ Freq)	Tramadol (Amt/Dose/ Freq)	IV Opioid (Dilaudid, Fentanyl,Morphine) (Amt/Dose/ Freq) **circle the name of drug**	Other Medication (specify) (Amt/Dose/ Freq))
1 hour						
4 hours						
8 hours						
12 hours						
24 hours						

Table 3: Adverse Events

Instructions: Please record any experienced adverse event on the respective time points.

Time Points	Nausea	Vomiting	Constipation	Somnolence	Dizziness	Fatigue	Other (specify)
1 hour							
4 hours							
8 hours							
12 hours							
24 hours							

Day 2:

Table 1: Numeric Pain Rating Scale

Instructions: Please record the number that best describes the level of pain (Figure 1) during rest and activity (raise both arms above the head and hold for five seconds) on the respective time points.

Time Points	Numeric Pain Scale (Rest)	Numeric Pain Scale (Activity)
36 hours (last 12 hours)		
48 hours (last 12 hours)		

Figure 1: Numeric Pain Rating Scale

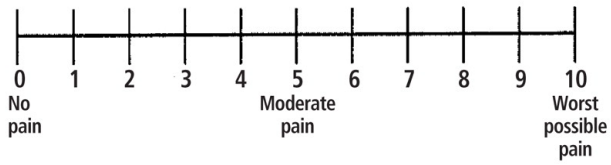


Table 2: Pain Medications

Instructions: Please record the amount & frequency of each medication that you have taken on the respective time points. Only include medications that were taken, since the last time point. Do not include medications already included in previous time points (even if they overlap).

Time Points	Tylenol (Amt/Dose/ Freq)	Percocet (Amt/Dose/ Freq)	Norco (Amt/Dose/ Freq)	Tramadol (Amt/Dose/ Freq)	IV Opioid (Dilaudid, Fentanyl,Morphine) (Amt/Dose/ Freq) **circle the name of drug**	Other Medication (specify)
36 hours (last 12 hours)						
48 hours (last 12 hours)						

Table 3: Adverse Events

Instructions: Please record any experienced adverse event on the respective time points.

Time Points	Nausea	Vomiting	Constipation	Somnolence	Dizziness	Fatigue	Other (specify)
36 hours (last 12 hours)							
48 hours (last 12 hours)							

Day 3:

Table 1: Numeric Pain Rating Scale

Instructions: Please record the number that best describes the level of pain (Figure 1) during rest and activity (raise both arms above the head and hold for five seconds) on the respective time points.

Time Points	Numeric Pain Scale (Rest)	Numeric Pain Scale (Activity)
60 hours (last 12 hours)		
72 hours (last 12 hours)		

Figure 1: Numeric Pain Rating Scale

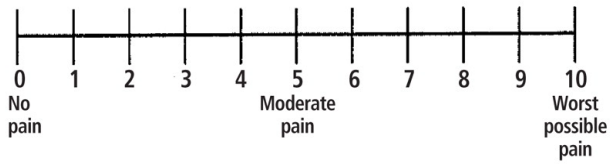


Table 2: Pain Medications

Instructions: Please record the amount & frequency of each medication that you have taken on the respective time points. Only include medications that were taken, since the last time point. Do not include medications already included in previous time points (even if they overlap).

Time Points	Tylenol (Amt/Dose/ Freq)	Percocet ((Amt/Dose/ Freq)	Norco ((Amt/Dose / Freq)	Tramadol (Amt/Dose/ Freq)	IV Opioid (Dilaudid, Fentanyl,Morphine) (Amt/Dose/ Freq) **circle the name of drug**	Other Medications (specify)
60 hours (last 12 hours)						
72 hours (last 12 hours)						

Table 3: Adverse Events

Instructions: Please record any experienced adverse event on the respective time points.

Time Points	Nausea	Vomiting	Constipation	Somnolence	Dizziness	Fatigue	Other (specify)
60 hours (last 12 hours)							
72 hours (last 12 hours)							

Day 4:

Table 1: Numeric Pain Rating Scale

Instructions: Please record the number that best describes the level of pain (Figure 1) during rest and activity (raise both arms above the head and hold for five seconds) on the respective time points.

Time Points	Numeric Pain Scale (Rest)	Numeric Pain Scale (Activity)
84 hours (last 12 hours)		
96 hours (last 12 hours)		

Figure 1: Numeric Pain Rating Scale

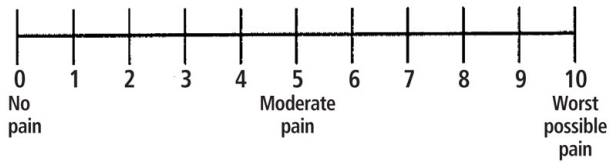


Table 2: Pain Medications

Instructions: Please record the amount & frequency of each medication that you have taken on the respective time points. Only include medications that were taken, since the last time point. Do not include medications already included in previous time points (even if they overlap).

Time Points	Tylenol (Amt/Dose/ Freq)	Percocet (Amt/Dose/ Freq)	Norco (Amt/Dose/ Freq)	Tramadol (Amt/Dose/ Freq)	IV Opioid (Dilaudid, Fentanyl,Morphine) (Amt/Dose/ Freq) **circle the name of drug**	Other Medication (specify)
84 hours (last 12 hours)						
96 hours (last 12 hours)						

Table 3: Adverse Events

Instructions: Please record any experienced adverse event on the respective time points.

Time Points	Nausea	Vomiting	Constipation	Somnolence	Dizziness	Fatigue	Other (specify)
84 hours (last 12 hours)							
96 hours (last 12 hours)							

Table 4: Patient Satisfaction:

Instructions: Please circle the number that best describes the degree of satisfaction you experienced with the pain medication provided to you during the last 4 days after surgery.

1- Very Unsatisfied 2- Unsatisfied 3- Neutral 4- Satisfied 5-Very Satisfied

Appendix 2- Brief Pain Inventory

Name:

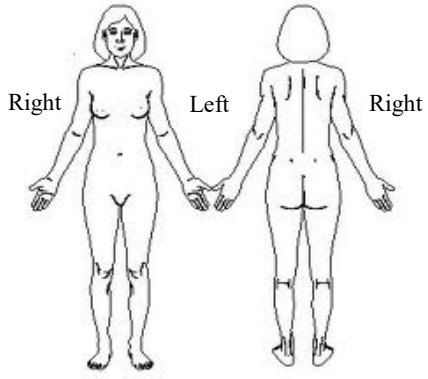
Subject #:

Brief Pain Inventory

1) Throughout our lives, most of us have had experience pain before (e.g. minor headaches, sprains, toothaches.) Have you had pain other than these kinds of pain today? (Circle Answer)

   Yes No

2) On the diagram, **circle** the areas where you feel pain. Put an **X** on the area that hurts the most.



3) Circle the number that best describes your pain at its **worst** in the past **24 hours**.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain Worst Pain

4) Circle the number that best describes your pain at its **least** in the past **24 hours.**

   0 1 2 3 4 5 6 7 8 9 10

   No Pain Worst Pain

5) Circle the number that best describes your pain on the **average**.

   0 1 2 3 4 5 6 7 8 9 10

   No Pain Worst Pain

6) Circle the number that best describes the pain you have **right now**

   0 1 2 3 4 5 6 7 8 9 10

   No Pain Worst Pain

7) What treatments/medications are you receiving for your pain?

   _____

8) Circle the percentage that most shows how much relief have pain medications provided.

0% 10 20 30 40 50 60 70 80 90 100%

No Relief — Worst Pain

9) Circle the number that best describes how, during the past 24 hours, pain has interfered with:

A. General Activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

C. Walking Ability

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

D. Work (outside home & housework)

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

E. Relation with other people

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

G. Enjoyment of Life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere — Completely interferes

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