Title of Study: Regional nerve blocks in alloplastic breast reconstructive surgery: A pilot, randomized controlled trial

Project Nickname: Nerve blocks in alloplastic breast reconstruction

Principal Investigator:
Kathryn Isaac, MD, MPH, FRCSC
UBC Department of Surgery, Mount Saint Joseph Hospital
604-336-9488

Co-Investigator(s):
Rebecca Warburton, MD, FRCSC
UBC Department of Surgery, Mount Saint Joseph Hospital
604-977-8511

Christopher Prabhakar, MD, FRCPC, CCFP
UBC Department of Anesthesiology, Mount Saint Joseph Hospital
604-806-8337 ext 62813

Lisa Li, MD, FRCSC
UBC Department of Anesthesiology, Mount Saint Joseph Hospital

Nancy Van Laeken, MD, FRCSC
UBC Department of Surgery, Mount Saint Joseph Hospital

Esta Bovill, MD, PhD, FRCSC
UBC Department of Surgery, Mount Saint Joseph Hospital

Primary Contact:
Caroline Illmann, MSc, Clinical Research Coordinator, UBC Division of Plastic Surgery

Additional Team Members:
Nicole Steinbrecher, BSc, BScN, UBC MD Candidate 2022

Anne Nguyen, BSc, MSc, MD, Clinical Research Associate, PHC Department of Surgery

Fagun Jain, MSc, Clinical Research Coordinator, UBC Division of Plastic Surgery

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Short Summary (<100 words): *(94 words)*
Pain management is a major concern in oncologic breast surgery and reconstruction. Significant risks for acute and chronic pain after surgery might be reduced through improved pain control pre-operatively. Addition of regional anesthesia to a multimodal peri-operative pain management protocol offers a promising solution for improved recovery. For patients undergoing mastectomy with immediate alloplastic breast reconstruction, this RCT compares Thoracic Paravertebral+Pec I local anesthetic block with a placebo normal saline block for their effect on acute pain, chronic pain, opioid consumption, opioid-related side effects, patient-reported quality of recovery after surgery, and length of stay.

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SECTION 1: INTRODUCTION (back)

Background/Justification

Breast cancer is the most commonly diagnosed cancer in females in Canada, making up 25% of all cancers diagnosed in this population.[1] When surgical treatment necessitates a mastectomy, immediate breast reconstruction (IBR) is a safe option for patients with early stage cancer.[2] Options for breast reconstruction include autologous tissue or alloplastic reconstruction with a prosthesis (insertion of tissue expander or immediate insertion of implant). In Canada, rates of IBR are increasing, with approximately 15-40% of breast cancer patients undergoing reconstruction in British Columbia.[3] Alloplastic reconstruction (with tissue expanders and implants) accounts for the majority of reconstructions in North America and is associated with more pain than autologous forms of breast reconstruction.[4-9]

Importantly, acute and chronic pain can be a major factor in patient recovery after breast reconstruction surgery.[10] Approximately 40%-47% of patients undergoing breast surgery experience significant acute postoperative pain.[5,11] Severe acute postoperative pain increases the likelihood of chronic pain in the breast and ipsilateral arm.[12] Chronic postoperative pain, defined as pain that persists after 3-6 months after surgical intervention, hinders survivor recovery, reducing productivity and overall quality of life.[13,14] One year after surgery, approximately 50% of patients who had a mastectomy and reconstruction experience pain compared to 30% of women who had a mastectomy without reconstruction.[5,15-17] Recent population cohort studies report little improvement in the incidence of chronic post-mastectomy pain, estimating 40-50% of patients suffer with resultant decrease in quality of life.[12,16,17]

Within alloplastic reconstruction, the use of tissue expanders increases the use of opioid and non-opioid analgesia as compared to the immediate insertion of an implant.[6] Predictive risk factors have been identified for developing chronic pain after breast surgery. Psychosocial and patient factors include baseline preoperative anxiety, depression, high BMI, younger age (<40), and catastrophizing.[18,19] Surgical factors include severe acute post-operative pain, axillary surgery, and adjuvant radiotherapy.[12,18] These studies underscore the importance of adequate perioperative pain management to reduce the risk of chronic pain in the setting of specific prognostic factors and to improve overall recovery.

Evidence-based multimodal perioperative management protocols improve the quality and value of care delivered for breast reconstruction patients.[20-22] These Enhanced Recovery After Surgery (ERAS) protocols have been applied to patients undergoing mastectomy with immediate alloplastic breast reconstruction and successfully demonstrate benefits of decreased opioid usage, decreased acute post-operative pain, same-day discharge, patient satisfaction, and well-being.[20,21,23-25] In these published recommendations for optimal perioperative care, regional blocks of the chest are absent from the list of supported strategies due to lack of high-level evidence.[15,20,21,26] Recent systematic reviews and anesthesia guidelines support regional blocks as an important

adjunctive strategy to these multimodal perioperative protocols for patients undergoing major oncologic breast surgery and breast reconstruction.[26-28]

Regional blocks of the chest have the potential to decrease acute and chronic pain but are absent from the list of supported strategies due to lack of high-level evidence.[15,20,21,26] Recent meta-analysis, systematic reviews and anesthesia guidelines support regional blocks as an important adjunctive strategy to these multimodal perioperative protocols for patients undergoing major oncologic breast surgery and breast reconstruction.[26-29]

Regional anesthesia techniques in breast cancer surgery include thoracic epidural blocks, thoracic paravertebral blocks (TPVB), pectoralis (pecs) blocks and serratus anterior (SA) plane block. According to recent procedure-specific guidelines, TPVB are recommended for pain management after oncologic breast surgery as part of a multimodal perioperative protocol.[27] TPVB combined with general anesthesia (GA), as compared to GA alone, significantly reduce the worst postoperative pain scores in early postoperative period (<2h) (mean difference - 2.68; 95% CI:-3.33 to-2.02, p<0.00001).[29] While the TPVB provides superior analgesia, the pecs and SA blocks are less invasive, are effective adjuncts in pain management, and may have a superior safety profile.[15,28,30]

Oncologic breast surgery with and without reconstruction differs with respect to the pectoralis and serratus muscles. In alloplastic breast reconstruction, the pectoralis major muscle is disinserted and elevated to insert the prosthesis. The serratus fascia may also be elevated to support the soft tissue coverage of the prosthesis. This surgical dissection of pectoralis and serratus is absent in oncologic breast surgery without reconstruction. Pecs I and II, SA, and TPVB are indicated for alloplastic breast reconstruction.[26,31] The optimal regional block for alloplastic breast reconstruction is not known.

Current Approaches to Regional Blocks in Oncologic Breast Surgery & Reconstruction

1. Pecs Block **(back)**

The Pecs I block, first described by Blanco, involves injecting local anesthetic under ultrasound guidance into the interfascial plane between pectoralis major and minor.[32] Pecs I block is used to anesthetise the lateral and medial pectoral nerves. Pecs II block, also described by Blanco, involves injecting local anesthetic under ultrasound guidance above the SA muscle at the level of the third rib.[33] The technique includes and expands on the Pecs I block to target the pectoral, intercostobrachial, intercostals III-VI, and long thoracic nerves in addition to the lateral and medial pectoral nerves (which are blocked in Pecs I).[15] Both the pecs I and II blocks may be done as a single injection. The pecs blocks are simple to perform under ultrasound guidance, do not cause any sympathetic blockade, and are fast-acting.[15,28]

Two randomized controlled trials (RCTs) evaluating combined pecs I and II block demonstrated a reduction of intraoperative opioid consumption (mean total fentanyl consumption 141 +/- 32 ug intervention versus 218 +/- 24 ug control group, $p<0.001$), postoperative opioid consumption (mean total fentanyl consumption 438 +/- 72 intervention versus 609 +/- 53 ug control group, $p<0.001$), and lower pain scores for patients undergoing modified radical mastectomy compared to controls who received general anesthesia alone.[34,35] Reduced postoperative nausea, vomiting, sedation scores, and improved early shoulder mobility have also been reported for patients undergoing a pecs block compared to controls.[34]

The effect of Pecs II block in patients undergoing modified radical mastectomy with IBR with an implant and latissimus dorsi flap was assessed in a recent RCT.[36] Wang et al. found a significant reduction in intra- and postoperative opioid consumption, less postoperative nausea and vomiting, and reduced pain scores in the Pecs II with general anesthesia as compared to general anesthesia alone.

There are few studies comparing pecs I and pecs II blocks. One study compared pecs I to pecs II blocks using epidural catheters placed under direct vision intraoperatively during modified radical mastectomy surgery, and found that pecs II offered superior postoperative analgesia compared to pecs I.[37] There are no reported studies directly comparing pecs I to pecs II in breast reconstruction surgeries.

An important disadvantage of the Pecs II block is the disruption of the axillary tissue planes which can directly affect axillary surgery.[38] Furthermore, neural blockade of the long thoracic nerve and other axillary nerve branches with Pecs II block is problematic for axillary lymph node dissection when intra-operative nerve stimulation is used for identification and preservation.

2. Serratus Anterior Plane Block

The SA block involves ultrasound-guided injection of local anesthetic into the potential spaces superficial and deep to the SA muscle. It targets the thoracic intercostal nerves.[39] The SA block developed as a method to provide complete analgesia of the lateral thoracic cage as an alternative to the TPVB or thoracic epidural blocks. The SA block may be performed as a superficial or deep block (or both). The blocks are similar in terms of patient-reported pain postoperatively.[40,41] The superficial SA block may have less risk of pneumothorax, but both the superficial and deep SA blocks have a good safety profile.[38,40,42] The deep SA block is preferred for breast cancer surgeries involving the axillary or sentinel lymph nodes, as the anesthetic does not infiltrate the axillary tissue planes, unlike the superficial SA block.[40,42] The blocks are similar in their analgesic effect.[40,42]

Several studies support the role of the SA block with general anesthesia compared to general anesthesia alone. A recent RCT found the ultrasound-guided SA block with general anesthesia resulted in significantly lower opioid requirements intra- and

postoperatively, and no differences in complication rates or postoperative nausea and vomiting.[30] A second study comparing the deep SA block under direct visualization to general anesthesia alone found the SA block resulted in marginally lower pain scores, but notably with no reports of severe pain in the first 24 hours after surgery.[43] No adverse events related to the blocks were observed in this study. However, these preceding studies included fewer than 5 patients undergoing breast reconstruction.

Retrospective comparison of Pecs I, SA blocks, and controls in breast cancer surgery without reconstruction found that Pecs I and SA blocks each reduced postoperative opioid consumption and postoperative nausea and vomiting.[38]

3. Thoracic Paravertebral Block **(back)**

TPVB targets the spinal nerves as they emerge from the intervertebral foramina. Under ultrasound guidance, a needle is inserted lateral to the vertebral spinous processes to anesthetize single or multiple spinal nerves, resulting in anesthesia the corresponding dermatomes.

Based on multiple meta-analyses of randomized clinical trials, TPVB is considered to be one of the most effective blocks for long-lasting analgesia after breast cancer surgery.[15,27,29,44,45] In oncologic breast surgery, meta-analyses of TPVB with general anesthesia compared to general anesthesia alone support that TPVB with general anesthesia resulted in superior postoperative pain control.[27,29] TPVB alone has also been compared to general anesthesia with similar results, including lower pain scores, lower opioid consumption (RR 0.23, 95%CI 0.15-0.37), lower incidence of post-operative nausea and vomiting (RR 0.27; 95% CI 0.12-0.61), and shorter lengths of hospital stay.[44] TPVB has also been shown to reduce prevalence of chronic pain at one year following mastectomy with or without axillary surgery.[46]

For patients undergoing alloplastic IBR, observational studies support the use of TPVB compared to general anesthesia alone for reduction in LOS, opioid consumption, post-operative pain scores, and post-operative nausea and vomiting.[47-50] A single RCT in the setting of alloplastic reconstruction compared PVB with general anesthesia to general anesthesia alone.[51] In this non-blinded, non-placebo controlled RCT, the TPVB intervention resulted in a significant reduction in acute pain scores, total opioid administered, and total anti-emetics consumed. Patient-reported satisfaction and nausea and vomiting did not differ significantly between groups. This trial's study population was a heterogenous group that included reconstructive procedures without mastectomy or axillary surgery, did not blind exposure or outcome measures, and lacked a placebo control. Further high-level evidence and study is required to establish the value of TPVB in immediate alloplastic breast reconstruction.

Overall, ultrasound-guided TVPB is a safe approach with a complication rate of 0.70%.[52] Adverse events from the TPVB have been reported in meta-analyses of randomized clinical trials. Pooled analysis from 11 trials published 1999-2009 (reported

for 771 patients) revealed a very low relative risk of: Horner's syndrome (RR 0.05, CI 0.02 – 0.09), pneumothorax (RR 0.01, CI 0.02 – 0.03) post-operative nausea and vomiting (RR 0.26, CI 0.13 – 0.5), nerve damage (n=0), and vascular injury (n=0).[29] Failed anesthetic technique was the most common adverse event reported with a relative risk of 4.34 (CI 0.74 - 25.24).

Disadvantages of the TPVB includes poor anesthesia of the medial anterior chest and operator dependence, potentially influencing the efficacy and safety of the block.

Selecting the optimal regional block for Alloplastic Breast Reconstruction

There is growing evidence to support the addition of pecs I and SA blocks for mastectomy (with or without axillary surgery) with IBR using tissue expanders or immediate implants. Early case reports and subsequent series in breast surgery with and without reconstruction supported the combination of Pecs I and SA blocks resulting in lower opioid consumption.[53-56] A single RCT of combined Pecs I and SA blocks for modified radical mastectomy with axillary lymph node dissection and IBR reported reduced opioid consumption and decreased postoperative pain scores.[57] While promising, this trial did not specify the type of breast reconstruction performed.

Two RCTs found the Pecs II block resulted in improved postoperative analgesia and reduced opioid consumption compared to TPVB.[58,59] However, meta-analyses of 14 randomized trials comparing Pecs II and TPVB concluded that Pecs II and TPVB provide comparable analgesic effect.[60] Although Pecs II has merit, the disruption of axillary tissue as a result of Pecs II renders this regional block an inferior option for our surgical population which commonly requires sentinel lymph node biopsy or axillary dissection.[38]

There is a paucity of high-quality studies investigating the additional benefit of regional blocks for immediate breast reconstruction. Given the effectiveness and safety of TPVB, Pecs I and SA blocks in oncologic breast surgery, we sought to investigate the benefit of TVPB with Pecs I block in the framework of a multimodal peri-operative management protocol. We have selected the most effective block in oncologic breast surgery, namely TPVB, and added the Pecs 1 (TPVB+) to provide the anesthesia required for the disruption of pectoralis muscle that occurs with immediate alloplastic breast reconstruction.

Hypothesis (back)

Local anesthetic regional blocks (LA blocks) of the thoracic paravertebral space and the pectoralis major (TPVB+) will reduce chronic pain.

Secondary hypotheses include: TPVB+ will decrease opioid consumption, postoperative nausea and vomiting, decrease patient-reported postoperative pain scores, length of stay, and improve patient-reported quality of recovery in patients undergoing total mastectomy with IBR using tissue expanders or immediate implants.

Objectives (back)

The primary objectives of the **pilot trial** are to demonstrate feasibility of recruitment and to demonstrate efficacy potential. The primary objectives of the **definitive trial** are to determine if Thoracic Paravertebral with Pecs 1 blocks (TPVB+) will reduce opioid consumption and chronic pain compared to a TPVB+ sham block in patients undergoing mastectomy with IBR using tissue expanders or implants. Secondary objectives of the definitive trial include assessment of opioid consumption, patient-reported postoperative pain scores, postoperative nausea and vomiting, length of stay, and patient-reported quality of recovery.

Significance (back)

The definitive trial will determine if TPVB+ improves postoperative acute and chronic pain and reduces opioid use for patients undergoing mastectomy with IBR using tissue expanders or immediate implants.

International Consensus guidelines for ERAS in breast reconstruction make a strong recommendation for multimodal, opioid-sparing analgesia postoperatively based on high-level evidence.[22] Increased total opioid analgesic use has been shown to increase length of stay in hospital.[25] Reduced opioid consumption results in less postoperative nausea, vomiting, and constipation, supports early ambulation, shortens hospital stays, and improves psychological well being.[21] Current ERAS protocols for alloplastic breast reconstruction are successfully opioid-sparing and address acute recovery.[21,25] However, opioids continue to play an important role in peri-operative protocols for achieving adequate pain control, which suggests further adjunctive strategies may be beneficial. Furthermore, the effects of peri-operative protocols on the development of chronic pain are lacking. By evaluating the effectiveness of TPVB+ in alloplastic reconstruction, our proposed study would help to establish an important additional feature to the ERAS pathway for our hospital and other institutions.

Furthermore, the COVID-19 pandemic has caused an unprecedented shift in pressures facing our healthcare system. Operating room closures and pauses in screening for certain conditions (eg. mammography for breast cancer) in the spring of 2020 resulted in a backlog of an estimated 30,298 surgical cases.[61] As British Columbia enters a phase of surgical renewal to meet patient demand, finding ways to limit use of in-patient resources while providing safe surgical care remains more important than ever. In this context, the use of regional anesthesia such as the TPVB+ block is very timely. By enhancing multimodal perioperative analgesia, the TPVB+ block may reduce perioperative and postoperative opioid requirements, reduce patient symptoms that could delay discharge, and shorten overall length of hospital stay. This could maximize the efficient use of needed surgical resources, while preserving inpatient resources for treatment of COVID-19 patients.

Benefits for Patients

Patients may benefit from LA blocks (TPVB+) by requiring less total opioid analgesia in the perioperative period. Patients may report reduced postoperative pain scores, and may experience fewer side effects related to opioid consumption (nausea and vomiting). This may result in a shorter length of stay in hospital and improved overall quality of recovery. Furthermore, the reduction in acute pain may reduce the incidence of chronic pain.

The use of regional anesthesia (rather than general anesthesia alone) may reduce recurrent breast cancer risk, although this is currently under investigation.[62,63]

Benefits for Researchers

The benefit to the plastic surgeon, general surgeon, and anesthesiologist will be knowledge of the patient-reported effectiveness as well as the postoperative and long-term morbidity of LA blocks as measured by total opioid analgesia in the perioperative period, patient-reported postoperative pain scores, side effects related to opioid consumption, reported quality of recovery and incidence of chronic pain. There may be an additional benefit of shorter length of stay in hospital, which has positive implications both for patients and for improved resource allocation within the health care system.

SECTION 2: METHODS (back)

Study Design (back)

The design of the pilot RCT is the same as the future definitive trial, a parallel-group, double-blinded randomized controlled trial (RCT). The target population are patients undergoing mastectomy with IBR using tissue expanders or immediate implants. The intervention will be a local anesthetic regional block defined as a TPVB with Pecs 1 (TPVB+) using local anesthetic infiltrate. The local anesthetic block (LA block) will be compared to a placebo block (sham block) using normal saline infiltrate. Thus, each patient in this study will be assigned to receive either; 1) LA Block: TPVB and Pecs I block with local anesthetic infiltrate, or 2) sham block: TPVB and Pecs I block with saline infiltrate. The assignment of intervention will be determined by randomization through REDCap. The pilot trial will be conducted at Mount Saint Joseph Hospital (MSJH).

Each participant will be assigned a consecutive Study ID at time of enrollment. Patients will be randomized 1:1 to either LA or sham block. Patients undergoing symmetrizing procedures as part of a bilateral breast surgery will not have a regional block on the symmetrizing side (which is not IBR). Patients undergoing bilateral IBR surgery using implants or expanders on both breasts will not be included in the study due to risk of local anesthetic toxicity with bilateral TPVB+.

The randomization sequence will be created using REDCap-generated 1:1 randomization with permuted blocks of varying size (4 and 6). The assignments (LA or sham) will be placed in order in opaque, consecutively numbered envelopes. The sequence and envelopes will be created by an independent research assistant who will not be involved in the remainder of the study implementation.

Study participants, Operating Room (OR) anesthesiologists, surgeons, research assistants, and nurses in the OR, Post-anesthesia Care Unit (PACU), and ward will be blinded as to whether a participant receives LA block or sham block. At MSJH, the anesthesiologists in the operative theater are separate from the team of regional anesthesiologists performing regional blocks in the preoperative area. Only the regional anesthesiologist and anesthesia assistant in the preoperative block area will be unblinded to reduce the potential unnecessary risk of a pneumothorax with the sham saline TPVB. This will enable injection of saline just outside of the paravertebral space.

On the day of surgery, the regional anesthesiologist at MSJH will be provided with the Study ID specific sealed envelope which will assign the patient to receive either the LA block or sham block. The regional anesthesiologist will prepare local anesthetic or normal saline injections for infiltration based on the random assignment. For all patients, the regional block will be performed as outlined in the Procedure Protocols (See Appendix 1: Nerve Block). The regional anesthesiologist will be unblinded and will therefore be able to purposefully inject the saline block in a safe plane outside of the paravertebral space to further reduce the risk of pneumothorax. All other parameters and protocols will be identical.

Currently, at MSJH, approximately 4 - 5 cases of mastectomy with IBR are performed per week. We do not anticipate difficulty with enrolment into this study. This internal pilot will generate initial recruitment data to enable an early review and validation of our recruitment projections and study population target prior to transition to formal RCT.

Study Setting (back)

The pilot trial will take place at MSJH in Vancouver, BC. Study enrolment and all subsequent study activities will take place on site at MSJH. The planned timeline for recruitment into the study is one year from REB approval (tentatively December 2020).

Inclusion Criteria (back)

1- Patients must be female, and at least 19 years old.
2- Patients must be ASA grade I or II.
3- Patients must be undergoing total mastectomy with IBR using tissue expander or implant, with or without axillary surgery.

Exclusion Criteria (back)

Patients will be excluded if:

1- Patients have a known contraindication for a regional block: known coagulation disorder, treatment with anticoagulants, infection at the injection site, known allergy to medication in the study.
2- Patients who are pregnant at the time of surgery.
3- Patients having bilateral mastectomy and immediate alloplastic breast reconstruction (as only one side can be blocked to prevent local anesthesia toxicity).
4- Patients with ASA Class III or IV.
5- Patients with BMI>35kg/m^2.
6- Patients weighing less than 50kg.
7- Patients living/staying outside of 1-hour driving distance from hospital.

Recruitment (back)

Plastic surgeons will identify potential eligible candidates for this study once they have consented for mastectomy with alloplastic IBR. Plastic surgeons will have adequate information after consultation to indicate whether the patient meets eligibility criteria. For potential participants who meet eligibility criteria, the plastic surgeon will introduce the study. The list of eligible potential participants will be emailed by the surgeon to the research assistant. Plastic surgeon will not be directly involved with recruitment and consent process.

The research assistant will be responsible for sending introductory materials package to the participants. The introductory materials package include an Initial Contact Letter (see Form 1), Consent Form (see Form 2), Nerve Block Information (see Form 3), Intake Form and Quality of Recovery-15 Questionnaire (baseline) (see Form 4). The package will be emailed to the patients as well as sent out through mail.

Patients who have received the Initial Contact Letter and have not declined to participate will be called by the research assistant 2-5 days after the email is sent out. Patients who do not have an email will be called 7-10 days after the mail is sent. All patient contact by the research assistant will be documented on Form 9: Recruitment Log. At this time, the research assistant will provide general information about the regional block study and confirm eligibility of the participant based on inclusion and exclusion criteria. If the patient is an eligible candidate, the research assistant will then provide a detailed description of the trial.

If the patient is interested in participating in the study, the research assistant will discuss the study Consent Form with the patient and will provide an opportunity for the patient to ask any questions about the study before their surgery date. Verbal telephone consent will be documented in the Recruitment Log. If the patient expresses verbal consent to participate in the study, the research assistant will ask the patient to complete the Intake

Form and Quality of Recovery-15 Questionnaire (baseline) prior to the day of surgery. They will be asked to bring the forms along with the signed consent form on the day of the surgery.

Research Assistants will call a day prior to the surgery to remind patients to complete the Intake Form and Quality of Recovery-15 Questionnaire (baseline) (Form 4) and bring these forms along with the Consent Form, on the day of surgery. Research assistants will answer any additional questions.

On the day of surgery, the patient will meet with the research coordinator and sign the Consent Form to confirm their participation in the trial. Only once the Consent Form is signed will the collection of data begin.

After signing the Consent Form, participants will receive a study ID number (i.e. NB01). The study ID number will be computer generated. The research assistant will match participant names to study ID numbers in a password-protected, encrypted Code Break linking list (Form 10) at the time of obtaining consent for participation in the study. Intake Form and Quality of Recovery-15 Questionnaire (baseline) (Form 4) will be collected by the research coordinator at this time.

Patients who decline to participate in the study on the day of surgery will not receive a sham or local anesthetic regional block. These patients will receive the current standard of surgical care at MSJH. Current standard of care is an evidenced-based multimodal perioperative regime for optimizing recovery after surgery and General Anesthesia. Standard of care does not include routine use of regional blocks (see Appendix 2), however patients may request the regional block from the anesthesiologist.

Participants will have their surgery scheduled within 2 months of enrolment. Involvement in the study will not affect the scheduling of surgery dates. Both participants and non-participants will experience the same surgical timelines between their preoperative consults and their date of surgery.

Outcome Measures **(back)**

Primary outcomes of the pilot trial: To demonstrate a reduction in chronic pain at 3 and 6 months from 50% to 30% would require approximately 220 patients assuming $\alpha = 0.05$ (2-sided), $\beta=0.15$. Before embarking on a definitive multi-centre trial it is important to demonstrate feasibility and potential efficacy.[64]

Feasibility: The definitive trial will be considered feasible if 1) > 50% of eligible patients are enrolled, 2) > 90% of blocks are successful, 3) retention at 6 months is > 90%.

Preliminary evidence of efficacy: Although severe acute post-operative pain is not the only risk factor for chronic post-surgical pain (CPSP), an intervention that does not decrease postoperative pain is unlikely to have a significant impact on CPSP. If the 80%

confidence interval for the between-group difference in average pain score in the 24-hour postoperative period favours LA block, we will consider that preliminary evidence of efficacy.[65,66]

Secondary outcomes of the pilot trial include adverse events related to study interventions. We will also collect the outcomes for the definitive trial to test and refine data collection processes.

The primary outcome in the definitive trial is chronic pain, defined by the Pain Burden Index, measured at 3 and 6 months following surgery. The Pain burden Index examines postsurgical pain in four postoperative body areas. The Index is calculated as a sum of the four locations (breast, chest, axilla, arm) multiplied by the frequency of pain[12] (see Form 8: Pain Burden Index).

Secondary outcomes of the definitive trial include:

- Opioid analgesia requirements during surgery and in the first 24 hours after surgery, defined as morphine milligram equivalents (MME). The total MME will include intraoperative opioids administered in the OR and postoperative opioids administered/ingested in the Postanesthetic Care Unit (PACU), Surgical Day Care Unit (SDC), Inpatient Unit, and home in the 24-hour period after completion of surgery. Opioids consumed will be converted to MME (see Appendix 3: Calculation of Morphine Milligram Equivalents (MME)).

- Acute patient-reported pain scores:
    - Numerical Rating Scale (NRS; 11-point scale) measured at the standard time points of nursing care assessments: preoperatively (baseline); four times per hour in PACU until discharge; if admitted, hourly for 2 hours, and then every 6 hours in the Inpatient Unit; and at discharge from hospital; 24 hours after surgery is complete.

- Opioid-induced side effects:
    - Postoperative nausea and vomiting
        - Nausea severity (by Verbal Rating Scale) in PACU
        - Vomiting episodes (0-48 hours after surgery) in PACU & home

- Quality of recovery (Form 7: Quality of Recovery-15 Questionnaire)
    - Measured with the Quality of Recovery-15 (QoR-15) scores at baseline prior to surgery and 24 hours after surgery[67-69]. This 15-item questionnaire assesses patient-reported pain, physical comfort, physical independence, psychological support, and emotional state.[69] It takes an average of 2.5 minutes to complete. The QoR-15 has been statistically validated and is designed for both ambulatory and inpatient surgery populations.[68,70]

- Length of stay (LOS) in hours in hospital

    - Measured from the time admitted to PACU to the time discharged from hospital. LOS includes time in the PACU, Surgical Day Care (SDC) and, if required, Inpatient Unit. Patients are transferred between units and discharged from hospital according to standardized institutional criteria (see Appendix 4: PACU and SDC Discharge criteria).

- Time-based outcome measures:
    - time to perform ultrasound-guided TPVB+
    - time under general anesthesia
    - time in PACU
    - failure of discharge from PACU and requiring admission

- Rescue medications:
    - Need for rescue opioid analgesics and anti-emetics
        - Rescue medications are defined as those required "as needed" (ie. beyond scheduled) in the PACU, ward, and after discharge
    - Time to rescue opioid analgesics and anti-emetics

- Failure of early discharge:
    - Emergency room visits within 48 hours of discharge

- Complications and adverse events
    - Related to the ultrasound-guided regional block: vascular or nerve injury, Horner's syndrome, bleeding/hematoma, local anesthetic systemic toxicity, pneumothorax, distortion tissue planes during axillary dissection, and other.
    - Related to the surgery: hematoma, tissue necrosis, urgent unplanned return to the operative theater within 24 hours of surgery.

These measures are listed in Form 6: Clinical Form and Form 11: Data Collection Form.

Sample Size

240 IBR procedures are performed annually at MSJH, 50% participation yields ~ 30 patients in 3 months. Assuming a difference of 1 and standard deviation of 1.2, this sample size yields > 80% probability that the lower bound will exclude 0.[45]

Additional Details of Study Design

Participants will also be given at the time of consent a post operative package. This will contain the Quality of Recovery-15 Questionnaire (Form 7), Recovery Booklet (Form 5) and Pain Burden Index (Form 8).

The Quality of Recovery-15 Questionnaire (see Form 7) is to be completed at 24 hours after surgery in paper format or electronic format (based on their preference). This

24 hour time point will be marked on the QoR-15 form. If paper format is preferred, the QoR-15 will be provided with a paid-postage envelope to return once completed at 24 hours after surgery. The pain NRS at 24 hours will be recorded from the chart. The envelopes will be addressed to the research coordinator at UBC Hospital office. If the participant prefers electronic format, the questionnaire will be sent to their provided email address using secure online format (REDCap developed questionnaire).

Recovery Booklet (see Form 5) will include: a) schedule for taking prescription pain medications; b) a postoperative 7-day symptom diary (for recording pain on NRS at 24 hours, episodes of vomiting, nausea, and use of prescribed medications). Patients will be provided with a paid-postage envelope to return their Recovery Booklet via mail once completed at 7 days after surgery. Patients will be reminded to complete the Recovery Booklet (Form 5) in 3-4 days and once again at 14 days to return the envelope.

The Pain Burden Index questionnaire (see Form 8) asks specifically about pain in four surgically related body areas and to calculate the Pain Burden Index (PBI). The PBI is calculated by summing the pain severity scale (0–10) at each of four locations (breast, axilla, chest wall, arm) multiplied by the frequency of the pain at each site. The PBI questionnaire will be sent to participants via mail as paper format (with paid-postage envelope to return once completed) or email as electronic format (as per their requested preference) to be completed 3 and 6 months after their surgery. Details of present adjuvant treatments (radiation and chemotherapy) will also be included in the questionnaire.

Secondary outcomes data including opioid consumption and side effects, length of stay in hospital (hours), rescue medications, failure of early discharge, complications and adverse events and time-based outcome measures (time in PACU, time under general anesthesia, time to perform ultrasound-guided TPVB+, failure of discharge from PACU and requiring admission) will be collected through participants' charts and EMR.

Risk/Benefit Estimates **(back)**

Anticipated Benefits to Participants

Participants will be randomly assigned to receive TPVB+ nerve blocks with either local anesthetic or sham (saline) followed by general anesthesia.

Participants who are randomly assigned to saline infiltration for TPVB+ may not notice any improvement in postoperative pain scores, opioid requirements, side effects related to opioid consumption (eg. nausea and vomiting), chronic pain, or shortening of hospital stay.

Participants who are randomly assigned to local anesthetic infiltration for TPVB+ may report reduced postoperative pain scores, require less total opioid analgesics or other medications in the perioperative period. Participants may experience fewer side effects

related to opioid consumption (eg. nausea and vomiting), may have lower risk of chronic pain, and may have shorter lengths of stay in hospital.

All participants will be asked to reflect on their recovery and pain when completing the QoR-15 and PBI questionnaires. If appropriate, any issues flagged through completion of the QoR-15 or PBI questionnaire may be addressed to optimize participant recovery and optimize chronic pain control.

Potential Harms or Risks to Participants

Participants randomly assigned to the sham or local anesthetic TPVB+ followed by general anesthesia will be exposed to risks associated with the administration of regional blocks, such as (but not limited to) pain or discomfort at the time of the injection, hematoma, or pneumothorax.

Adverse events from the TPVB have been reported in meta-analyses of randomized clinical trials. Failed anesthetic technique was the most common adverse event reported with a relative risk of 4.34 (CI 0.74 - 25.24).[29] Other adverse events were rare with low relative risks: pneumothorax (RR 0.01, CI 0.02 – 0.03, occurs in 1 in 600 cases); post-operative nausea and vomiting (RR 0.26, CI 0.13 – 0.5); nerve damage (n=0), and vascular injury (n=0).[29] Horner's syndrome (sympathetic blockade) has occurred in less than 1 in 100 cases.[29] Nerve damage and vascular injury have a theoretical risk of 1 in over 1000 cases.[29] Local infection has a theoretical risk of 1 in 2500 cases.[71] Horner's syndrome (temporary small pupil and droopy eyelid) has occurred in less than 1 of 100 cases.[29]

Participants receiving the saline TPVB+ may not experience improved pain scores or reduced opioid consumption postoperatively, unlike what is expected for participants receiving a local anesthetic regional block.

Participants in this study, as compared to those not receiving regional anesthesia, may have an additional risk of Local Anesthetic Systemic Toxicity (LAST, a serious adverse reaction to local anesthetic occurring in less than 1 in 12,000 cases[72]), or other risks specific to the injection of local anesthetic.

Risk/benefit discussions with prospective participants will occur at the time of consent for the study and participants will also have the opportunity during the PAC call/visit and on day of surgery to ask the anesthesiologist questions regarding the regional block procedure. Participants may contact the research assistant at any time before their surgery date with questions regarding the regional block procedure. Questions beyond the scope or knowledge of the research assistant will be forwarded to the appropriate study physician with expertise in anesthesiology or surgery.

Assessment of Safety

The safety of the TPVB+ have been established in the literature. There are rare complications associated with the blocks which will be clearly defined and outlined to the

participant during the recruitment phase of the study. The participant will have two separate occasions to ask the medical team and trained anesthesiologist for details on the regional anesthesia: during the PAC visit/phone call and preoperatively on the day of surgery. The TPVB+ will be performed by a consistent group of trained regional anesthesiologists.

Adverse Events

Adverse events related to study interventions (TPVB+) will be recorded and tracked as per the study Data Collection Form on REDCap.

Statistical Analysis **(back)**

Patient characteristics and outcome measures will be summarized by group. An 80% confidence interval for the difference in average pain score over 24 hours will be calculated.

Quality Control and Assurance

All staff anticipated to be involved in the study, including anesthesiologists, general surgeons, plastic surgeons, research assistants, and nursing staff will be notified about the study and educated as appropriate on study interventions, data collection, and participant confidentiality. All staff providing study interventions (regional blocks), surgery, or perioperative care will be educated on relevant study outcomes being monitored.

Protocols have been prepared for the study interventions to ensure a standardized approach (Appendix 1: Nerve Block Protocol; Appendix 2: Evidenced-Based Multimodal Perioperative Management Protocol for Alloplastic Immediate Breast Reconstruction; Appendix 4: PACU and SDC Discharge criteria; Appendix 5: Study Timeline). Standardized intake forms, clinical forms and participant questionnaires will be used to ensure that equivalent data is being collected for all participants (see Form 4: Intake Form, Form 5: Recovery Booklet, Form 6: Clinical Form, Form 7: Quality of Recovery-15 Questionnaire, Form 8: Pain Burden Index).

Detailed Research Protocols **(back)**

Please see Appendix 1: Nerve Block Protocol
Please see Appendix 2: Evidenced-Based Multimodal Perioperative Management Protocol for Alloplastic Immediate Breast Reconstruction
Please see Appendix 3: Calculation of Morphine Milligram Equivalents (MME)
Please see Appendix 4: PACU and SDC Discharge criteria
Please see Appendix 5: Study Timeline

Forms **(back)**

Please see Initial Contact Letter attached as **Form 1**.
Please see Consent Form attached as **Form 2**.
Please see Nerve Block Information attached as **Form 3.**
Please see Intake Form and Quality of Recovery-15 Questionnaire (baseline) attached as **Form 4**.
Please see Recovery Booklet attached as **Form 5**.
Please see Clinical Form attached as **Form 6**.
Please see Quality of Recovery-15 Questionnaire (24 hour follow-up) attached as **Form 7**.
Please see Pain Burden Index attached as **Form 8.**
Please see Recruitment Log attached as **Form 9**.
Please see Code Break linking list attached as **Form 10**.
Please see Data Collection Form attached as **Form 11**.
Please see Study Data Log attached as **Form 12.**

Data Collection

Data will be collected prospectively from the patients' chart on the day of surgery, If required, the EMR will be accessed to obtain additional details. After collection of all data during the inpatient stay, data will be recorded under the anonymized study ID number by the research assistant. With the study ID number, data will be entered into REDCap.

Participants will be randomly assigned to receive TPVB+ with local anesthetic or sham before general anesthesia. For all participants, data will be collected on the Intake Form, Clinical Form, Quality of Recovery-15 Questionnaire, Pain Burden Index, and Recovery Booklet in the following 7 sections:

1. The Intake Form will be completed by the patient during the initial contact phone call and includes information on general demographics and inclusion/exclusion criteria (without identifying information).
2. The first section of the Clinical Form will be used to record information on the perioperative course including the type of surgery performed: unilateral or bilateral; partial or total mastectomy with or without sentinel lymph node biopsy or axillary lymph node dissection; tissue expander or immediate implant reconstruction; adjunctive procedures will be recorded including biopsies and balancing reduction procedures.
3. The second section of the Clinical Form will record information on the general anesthesia provided; preoperative medications, intraoperative analgesics, sedatives, antiemetics, and anxiolytics. The form will also include details on the regional block and time to perform the block. Surgical and regional block complications within 24 hours of surgery will be recorded.
4. The third section of the Clinical Form will include information on participant-reported pain scores and medications in the postanesthetic care unit and inpatient ward.

5. The Quality of Recovery-15 Questionnaire will be completed by the participant at baseline before surgery and at 24 hours after surgery to evaluate the quality of their recovery.
6. The Recovery Booklet will be completed by the participant during the first 7 days after surgery to track scheduled and rescue medications required, opioid-related side effects (nausea and vomiting), and pain at 24 hours after surgery.
7. The Pain Burden Index will be completed by the participant 3 months and 6 months after surgery to evaluate for the presence and severity of chronic pain.

Confidentiality **(back)**

Management of Identifying Data:

Identifying information collected from potential participants includes: name, phone number/email (optional, only if provided by participant), age/date of birth, PHN, and mailing address. This identifying information will be stored in the Code Break. All potential participants will be assigned a Recruitment ID number (i.e. R01). The identifying information from potential participants who opt not to participate in this study will be deleted from the Code Break. After consent is obtained, each participant will be assigned a study number (i.e. NB01). This study ID number will be recorded in the Code Break. Identifying information will only be stored in the Code Break, with the exception of email on REDCap as outlined below.

The Code Break will be password-protected and stored on a secured UBC server. Email for the patients who opted for emailed surveys will be entered into REDCap.

The Consent Form will be stored in a locked secured filing cabinet in the Principal Investigator's (PI's) Office.

Management of Non-Identifying Data:

All non-identifying information collected will be kept on the completed Recruitment Log, Study Data Log, Intake Form, Clinical Form, Quality of Recovery-15 Questionnaire, Recovery Booklet, and Pain Burden Index as hard copies in a locked secured filing cabinet in the Principal Investigator's (PI's) office.

The Recruitment Log will record Recruitment ID number and consent progress. The Study Data Log containing tasks for research staff will be associated with Study ID number. The Recruitment Log and Study Data Log will not contain any identifying information.

The hard-copy Intake Form and the Baseline Quality of Recovery-15 (QoR-15) Questionnaire (Form 4) will be collected at the time of enrollment. An additional Quality of Recovery-15 (QoR-15) Questionnaire (Form 7) will be provided on the day of surgery to be completed 24 hours postoperatively, before discharge from hospital and then mailed

back. Both the Intake Form and the Quality of Recovery-15 (QoR-15) Questionnaires will be stored with the other hard-copy study forms in a locked secured filing cabinet in the PI's office.

The hard-copy Recovery Booklet (Form 5) will be given to participants and completed over the course of 7 days postoperatively, before discharge from hospital. The Recovery Booklet will be stored with the other hard-copy study forms in a locked secured filing cabinet in the PI's office.

Data collected on the day of the surgery (Clinical Form: 6) will be directly inserted into REDCap web application. Should any unforeseen circumstance make direct data entry unavailable on the day of surgery, hard copies of Form 6 will be used as a backup. This will also be stored in a locked secured filing cabinet in the PI's office

The Pain Burden Index questionnaire (Form 8) will be given to participants and completed at 3 and 6 months after surgery. The patient will receive the questionnaire 1 week before each of these dates and receive a phone call from the Research assistant to ensure receipt and answer any questions. The completed Pain Burden Index questionnaire will be stored with the other hard-copy study forms in a locked secured filing cabinet in the PI's office. If the patient prefers emailed questionnaires, the questionnaire will be completed using a secure online survey format and anonymized to their assigned study ID number.

The Data Collection Form outlines the variables and unit measures for the study and will not be used to store any data. Instead, participants' data from the Intake Form, Clinical Form, Quality of Recovery-15 Questionnaire, Recovery Booklet, Clinical Form and Pain Burden Index will be collected and entered into the REDCap server directly through a password-protected encrypted laptop. No identifying information will be stored on REDCap except for email of the patients who have opted for electronic surveys.

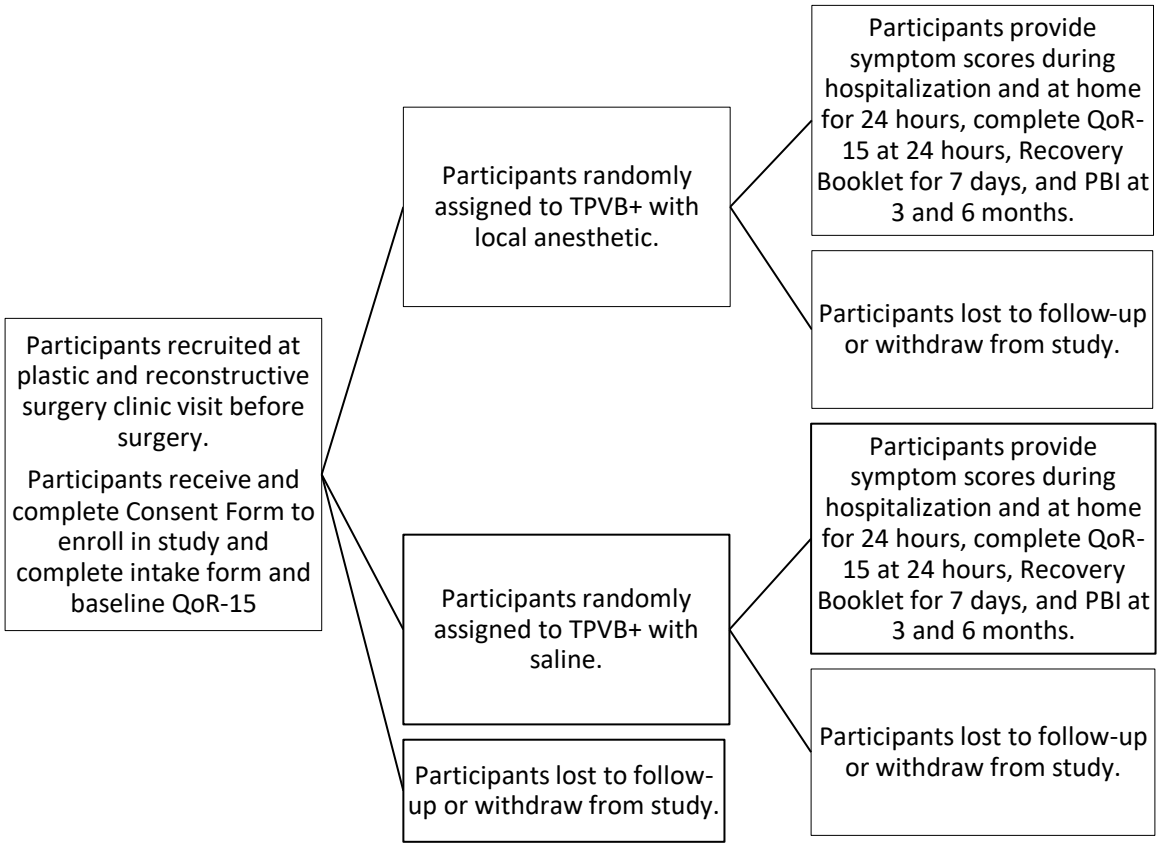
In summary, the Informed Consent, Intake Form, Clinical Form, Quality of Recovery-15 Questionnaire, Recovery Booklet, and Pain Burden Index will be kept as hard copies in the PI's office in a locked secured filing cabinet, separate from the Code Break linking list. Study Data Log and the Recruitment Log will be stored on the UBC server. All non-identifying data collected will be stored on REDCap. Since the Code Break is stored separately from clinical data collected on REDCap, there is minimal risk of linking participants' identifying information.

	Personal Identifying Information	Storage		
		Hard-Copy*	REDCap	Encrypted MS Excel Sheet†
Informed Consent Form (Form 2)	x	x		
Intake Form (Form 4)		x	x	
Recovery Booklet (Form 5)		x	x	
Clinical Form (Form 6)		x	x	
Quality of Recovery-15 Questionnaire (Form 7)		x	x	
Pain Burden Index (Form 8)		x	x	
Recruitment Log (Form 9)				x
Code Break (Form 10)	x			x
Study Data Log (Form 12)				x

***** Stored in Locked Cabinet in PI Office
† Password protected and stored on secure UBC server

Dissemination of Results
Results will be disseminated through manuscript publication in a peer-reviewed journal and presented at a plastic surgery, surgical oncology, or anesthesiology conference. Results will also be disseminated through hospital in-services, educational rounds, or CME presentations.

Project Timetable/Flowchart: (back)



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Appendix 1: Nerve Block Protocol: TPVB+ (TPVB with Pec I block) (back)

All sham and LA blocks will be performed by a regional anesthesiologist experienced in performing TPVB and Pec I blocks. The blocks will be performed in the preoperative block room. Participants will be monitored as per existing site policy. The blocks will be done using sterile technique. Before and after each procedure, the ultrasound machine will be cleaned and disinfected using disinfectant wipes and allowed to air dry as per hospital/site policy.

1. Prior to the procedure, the patient will have the procedure explained to them, and consent documented as per hospital policy. Standard monitors and a safety check will be performed. Sedation medication (midazolam 1-2mg and fentanyl 25-50mcg) will be given.
2. The regional anesthesiologist will prepare syringes for injection of sham and regional anesthetic blocks depending on patient allocation.
3. Syringes for injection may include:
    a. LA TPVB block: 25ml of 0.3% ropivacaine with 1:400K epinephrine
    b. LA Pecs I block:10ml of 0.3% ropivacaine with 1:400K epinephrine
    c. Sham TPVB block: 25ml normal saline (0.9% NaCl)
    d. Sham Pecs I block: 10ml normal saline (0.9% NaCl)
4. The skin at the planned injection site will be cleansed with 2% chlorhexidine solution or 1% iodine (10% povidone iodine) in case of chlorhexidine allergy.
5. Nonsterile conducting gel will be applied to the 9 MHz linear probe ultrasound transducer, and the transducer will be covered with a sterile drape.
6. The anesthesiologist will don a clean face mask and sterile gloves prior to handling sterile equipment or touching the sterile field.
7. Sterile ultrasound conducting gel will be applied to the skin.
8. Local anesthetic skin wheal will be raised with 1% lidocaine.
9. TPVB block: The T2/3 or 3/4 interspace will be determined by counting ribs with the ultrasound. The ultrasound probe will be place in a sagittal orientation aiming to visualize the transverse processes. The location of the pleura will be noted and the LA will be injected in the paravertebral space incrementally after negative aspiration looking for pleural drift. For the sham injection the needle will be inserted to just superficial to the transverse process for an erector spinae plane injection (between erector spinae muscles and the transverse processes).
10. Pecs I block: Infiltrate will be injected into the fascia between the pectoralis minor and pectoralis major muscles at the level of the 3rd rib in the mid-to-lateral 1/3 of the clavicle in a transverse to oblique orientation. Identification of the pectoral branch of the thoracoacromial artery will assist with needle placement. The needle will be inserted from medial/superior to lateral/inferior. Visual confirmation will be by ultrasound upon visualizing the separation of tissue layers with the injected infiltrate.
11. The needle and probe will be removed and the injection site wiped dry.
12. The patient will continuous monitored in the block area until ready for transport to the operating for surgery.

Appendix 2: Evidenced-Based Multimodal Perioperative Analgesia and Anti-emetic Management Protocol for Alloplastic Immediate Breast Reconstruction (back)

PREOPERATIVE

1- Patient Education:
   a. Information on options, risks/benefits, recovery [73-76]
2- Fasting & Nutrition:
   a. Allow clear fluids up to 2 hours before arrival to the hospital and no solid foods after midnight [26,77-79]
3- Preoperative Analgesics: [21] to be given in preop 30 minutes to 2 hours pre-induction
   a. Gabapentin 600mg po x1 [27,80-84]
   b. Acetaminophen 1000mg po x 1
   c. Celecoxib 400mg po x 1[21]
   d. Midazolam 1-4mg IV PRN during nerve block administration only
   e. Fentanyl 25-100mcg IV PRN during nerve block administration only
4- Preoperative anti-emetics: to be given in block room
   a. Dexamethasone 8mg IV [85-92]
      i. by Anesthesiologist in block room by slow infusion
5- Preoperative Antibiotics: to be given in block room
   a. Preoperative antibiotics within 60 minutes of incision [93]
      i. by Anesthesiologist in block room
6- Regional Anesthesia: Paravertebral block with Pecs I (TPVB+)[57,94] (Intervention)
   a. Paravertebral T3/4 block: 0.3% ropivacaine+1:400K epi x 25mL
   b. Pecs I block with 0.3% ropivacaine with 1:400 epi x 10mL
   c. TOTAL nerve block LA volume 0.3% ropivacaine x 35 mL = 105mg for 50kg patient

INTRAOPERATIVE

1- General Anesthesia
   a. Induction with Propofol (2-4mg/kg IV), Fentanyl (1-4mcg/kg IV), Rocuronium (0.5-1.2mg/kg IV)
   b. Endotracheal intubation
   c. Maintenance with inhalational Sevoflurane (0.6-1.2 MAC)
   d. Opioid as needed for hemodynamic stability (eg. Fentanyl 0.25-1mcg/kg IV boluses, Hydromorphone to maximum 2mg IV or Morphine to maximum 15mg IV)
   e. Ondansetron 4mg IV 30 mins before emergence from general anesthesia [85,86,88,95]
   f. Reversal of muscle relaxant at discretion of OR anesthesiologist with Neostigmine or Sugammadex IV
2- Sequential Compression Devices & Warming blanket
3- Breast block: 18cc of [0.25% bupivacaine with 1:400 000 epinephrine] diluted in 18cc of NS to give total volume of 36cc of [0.125% bupivacaine with 1:400 000 epinephrine] per patient prior to incision

POSTOPERATIVE (POSTANESTHETIC CARE UNIT)

1- Celecoxib 200mg po x1 [21]
2- Acetaminophen 1000mg PO q6h [96]
3- Ondansetron 4mg po/IV q6h
4- Gravol 25-50mg po/IV q4-6h PRN
5- Hydromorphone 0.2-0.4mg IV q5min PRN
6- Fentanyl 25mcg – 50mcg IV q15min PRN
7- Oxycodone 5mg-10mg po q4h PRN

POSTOPERATIVE (INPATIENT UNIT)

1- Celecoxib 200mg po bid for 2 doses [21]
2- Acetaminophen 1000mg PO q6h [96]
3- Ondansetron 4mg po/IV q6h for 72 hours
4- Gravol 25-50mg po/IV q4-6h PRN
5- Hydromorphone 0.2-0.4mg IV q5min PRN
6- Oxycodone 5mg-10mg po q4h PRN
7- Gabapentin 200mg po qhs [20,21]
8- Keflex 500mg po qid for 7 days

PRESCRIPTION (At discharge, as per instructions in Recovery Booklet)

1- Tramacet 1 – 2 tablets po q6h (40 tablets) [21]
   i. After Tramacet finished, Acetaminophen 500mg po qid
2- Celecoxib 200mg po bid for 2 doses [20]
   i. After celecoxib finished: Ibuprofen 400mg po tid [20,21]
   ii. Note: if discharge delayed, order for celecoxib adjusted for a maximum of 2 doses after discharge from PACU
3- Gabapentin 200mg po qhs for 2 doses [20,21]
   i. Note: if discharge delayed, order for gabapentin adjusted for a maximum of 2 doses after discharge from PACU
4- Ondansetron 4mg po qid for 72 hours
   i. Note: if discharge delayed, order for ondansetron adjusted for a maximum duration of 72 hours after discharge from PACU
5- Keflex 500mg po qid for 7 days
   i. Note: if discharge delayed, order adjusted to complete a 7-day course

Appendix 3: Calculation of Morphine Milligram Equivalents (MME) (back)

Opioid	**To convert to oral morphine milligram equivalent (MME), multiply dose of drug (in mg) by:***
Codeine	0.15
Hydromorphone	5
Morphine	1
Oxycodone	1.5
Tramadol	0.15
**Conversion ratios for opioids can vary based on individual patient drug metabolism, which may be influenced by genetics and other medications.*	
Fentanyl 0.01 (10mcg) IV = Equivalent to Morphine 5mg	

Table is adapted from National Guidelines for Opioid Conversion[97,98] and local Health Authority Opioid Conversion Table for Fentanyl.[99]

Appendix 4: PACU and SDC Discharge criteria (back)

PACU Discharge Criteria (1 of 2)

Assessment	Criteria
Neurological Function	• Orientated to person, place and time or orientation equivalent to patient's preoperative status. • Obeys commands. • Easy to rouse with a sedation score equal to or less than 2. • Adequate skeletal muscle tone as evidenced by: head lift sustained for minimum 5 seconds and moderate to strong handgrips (or preoperative equivalent). • Full movement and sensation to extremities following general anesthesia or preoperative equivalent.
Respiratory Function	• Intact protective airway reflexes: gag, swallow, cough, ability to clear secretions and no artificial airway in place. • Maintains patent airway independently for minimum 30 minutes post-extubation in PACU. • Spontaneous, regular, respirations at a rate 10 to 24/minute. • Maintains SpO_2 at 92% or greater on room air for a minimum of 15 minutes. • Oxygen order from anesthesia is required if patient is unable to maintain oxygen saturation at or above 92% on room air. • No O_2 adjustments for at least 15 minutes prior to discharge. **Exception: any patient with known or exhibiting signs of OSA will require assessment by anesthesia prior to discharge.**
Cardiovascular Function	• Blood pressure and heart rate are stable for 3 consecutive 15 minute assessments and within ± 20% of preoperative values. • Cardiac rhythm stable and equivalent to preoperative rhythm (if known). • Extremities warm with evidence of adequate tissue perfusion (or preoperative equivalent).
Thermoregulation	• Independently maintains temperature at minimum 36°C. • Temperatures exceeding 38.5°C require consultation with anesthesia prior to discharge.
Gastrointestinal	• Post operative nausea is absent or at a tolerable level to the patient following use of rescue anti-emetics/treatment. • If nasogastric tube present, tube is secure, patent and returns are appropriate, i.e. color, consistency and amount within expectation of surgery.

Table is adapted from Providence Health Care Nursing Standards, B-00-1310071- PACU Post Anesthesia Protocol, Published by Providence Health Care, January 2017.

Appendix 4: PACU and SDC Discharge criteria (continued)

PACU Discharge Criteria (2 of 2)

Urinary/Bladder	• Bladder non-distended or scanned bladder volume is less than 400 mL and no voiced complaints of bladder discomfort. • When urinary catheter in situ, minimum urine output 0.5 mL/kg/hr or as specified by anesthesia. • If urinary catheter present ensure ongoing need and secured with appropriate device. • Continuous bladder irrigation: ensure catheter is secured, patent, infusing correct solution and returns are prompt and appropriate.
Surgical Parameters	• Dressings and visible incisions are dry and intact with no evidence of active bleeding. • Drainage tubes are patent and secured with appropriate device. • Surgery specific parameters are consistent with surgery, anesthesia and patient's preoperative status (e.g. neurological/neurovascular function satisfactory, wound drainage appropriate, flap/graft perfusion adequate, etc.).
Comfort and Safety	• Pain is at a level acceptable to the patient, preferably at a pain score of 5 or less at rest on a scale of 0 to 10. • Insensate (blocked) limbs are secured in appropriate alignment and positioning.
Neuraxial (spinal and epidural)	• Able to tolerate head of bed at 30 degrees without hypotension or headache. • Motor block is at a score of 1 using Bromage scale – able to demonstrate knee bend and able to reposition self upright or to side for airway protection. • Spinal – sensory block is at T10 or lower **and** has regressed at least 2 dermatomes from the intraoperative state. • Epidural – sensory block is appropriate to location i.e. lumbar, thoracic and operative site.
Lines	Peripheral IV • Site satisfactory and dressing intact. • Patent with ordered IV fluid and rate infusing. • IV solution and new IV tubing labelled with date. • Extra IV sites removed if not needed. Note: 16 gauge IV's must be infusing fluid and cannot be saline locked. 14 gauge IV's must be removed prior to transfer to the ward. Central Line • Site satisfactory and dressing intact.

Table is adapted from Providence Health Care Nursing Standards, B-00-1310071- PACU Post Anesthesia Protocol, Published by Providence Health Care, January 2017.

Appendix 4: PACU and SDC Discharge criteria (continued)

SDC Discharge Score

DISCHARGE SCORE					
VITAL SIGNS	**TIME:**				
BP/P ± 20% Baseline	**2**				
BP/P ± 20-50% Baseline	**1**				
BP/P ± 50% Baseline	**0**				
ACTIVITY					
Able to ambulate	**2**				
Out of bed with assistance	**1**				
Unable to ambulate	**0**				
BLEEDING					
None / Minimal	**2**				
Medium Dressing less than 50% saturated	**1**				
Large Dressing more than 50% saturated or Hematoma	**0**				
PAIN (SCALE 0-10)					
None/Minimal	**2**				
Controlled with Medication	**1**				
Uncontrolled	**0**				
NAUSEA/VOMITING					
None/Minimal	**2**				
Controlled with Medication	**1**				
Uncontrolled	**0**				
TOTAL SCORES					
INITIALS					
∗ NOTE – Discharge criteria - Must score 8-10 with no score of Zero in any category					

Table is adapted from Providence Health Care Nursing Standards, Form PHC-PA 002, Surgical Day Care Postoperative record, Published by Providence Health Care, September 2017.

Appendix 5: Study Timeline (back)

Flow Diagram outlining the data collection timepoints.