A Comparison Study to Facilitate Earlier Discharge: Spinal Versus General Anesthesia for Outpatient Knee Surgeries, a Randomized Controlled Study

FUNDER: Department of Anesthesiology, Hospital for Special Surgery

PROTOCOL NO.: IRB #2017-1547

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PROTOCOL SYNOPSIS

Protocol Title:	A Comparison Study to Facilitate Earlier Discharge: Spinal Versus General Anesthesia for Outpatient Knee Surgeries, a Randomized Controlled Study
Protocol Number:	2017-1547
Protocol Date:	2/4/2021
Sponsor:	The Department of Anesthesiology, Hospital for Special Surgery
Principal Investigator:	David Kim, MD
Products:	2% preservative-free Chloroprocaine (Phase II); Mepivacaine (Phase II)
Objective:	Outpatient knee surgeries with duration of less than one hour poses a challenge to the use of spinal anesthesia given that traditional agents remain in effect for 2-3 hours, thus creating a mismatch between length of surgery and anesthetic resolution. Spinal mepivacaine is mostly used at our institution for these surgeries but the prolonged duration of the block in the PACU impedes earlier discharge. Patients do not like prolonged PACU stays due to slow recovery from spinal anesthesia. Many centers instead use general anesthesia (GA). While GA has the advantage of less surgery/anesthesia time ratio mismatch, the adverse effects of nausea, vomiting, prolonged emergence and pain control may contribute to lengthened discharge. Approved for spinal use in Europe in 2012, chloroprocaine is proven to be an effective local anesthetic with the advantage of faster block resolution, averaging 60 to 90 minutes. The intervention we are studying is whether chloroprocaine is a superior alternative to mepivacaine and general anesthesia in providing surgical anesthesia. We hypothesize that the use of chloroprocaine can combine the benefits of a short spinal anesthetic while avoiding the side effects of a general anesthetic, thus promoting earlier discharge.
Study Design:	Randomized Controlled Clinical Trial
Enrollment:	33/132
Subject Criteria:	1. Written informed consent obtained from subject and ability for subject to comply with the requirements of the study

	2. Subjects scheduled for knee arthroscopy that is anticipated to be less than one hour
	3. Age 18 to 80 years
	4. Ability to follow study protocol
	5. English speaking (secondary outcomes include questionnaires validated in English only)
Study Duration:	6/24/2018 – 2/4/2021
Data Collection:	• Collection timepoints: Pre-op, POD 0, POD 1, POD 3, POD 7 • Sources: EPIC, medical records, and patient
Outcome Parameters:	• The primary outcome will be time until ready for discharge, defined as duration from the PACU arrival to the time the patient has reached PADSS discharge criteria.
	• Secondary outcomes: induction time, time of emergence, time of resolution of spinal, time of ambulation, time of micturition, incidence of urinary retention, incidence of transient neurologic symptoms, incidence of neurologic deficits/neuropraxia, incidence of side effects related to spinal anesthesia, incidence of block failure, incidence of opioid related side effects, incidence of PDPH, incidence of emergence delirium /delayed emergence, incidence of sore throat, incidence of drowsiness, incidence of PONV, NRS Pain Scores, opioid consumption, time of discharge from PACU, time of meeting discharge criteria, patient satisfaction with intraoperative anesthesia and pain control, ORSDS, length of PACU stay, length of operative time, QoR-15.
Statistical Analysis:	Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.): 1. Three pairwise two-sample t-tests or Wilcoxon rank-sum tests 2. Alpha level: 0.05/3 = 0.0167 (two-sided) 3. Beta or power level: 80% power

1.0 INTRODUCTION

Ideally for ambulatory surgeries, the local anesthetic used for spinals would be safe with minimal side effects, be effective for surgical anesthesia, and be of short duration to not impede PACU discharges. For almost two decades, our department has been using mepivacaine as the local anesthetic of choice for shorter cases (duration of 150 minutes or less). It has fewer incidences of transient neurologic symptoms (TNS) in comparison to lidocaine, and is of shorter duration than bupivacaine. Recently, preservative-free chloroprocaine spinals have been reported to provide effective surgical anesthesia of 40 to 90 minutes (shorter than mepivacaine), depending on the dose given (30-60 mg), and have lower incidences of TNS (0-1.9%) than mepivacaine. It has been used as the safe and better alternative for short cases at other institutions. A recent randomized controlled trial compared 3 drugs for spinal anesthesia (chloroprocaine, lidocaine, bupivacaine) and found faster time until resolution of motor and sensory block with chloroprocaine (Teunkens et al RAPM 2016). This study involved 99 patients, and did not have a group of mepivacaine spinals, so there is still interest in comparing chloroprocaine in regards to safety and efficacy with the most commonly used local anesthetic used for ambulatory cases in our institution—mepivacaine.

Since June 2016, our department has been using 2-chloroprocaine for spinal anesthesia, specifically for cases of short duration (less than one hour). At several academic institutions in the U.S., including Columbia, Virginia Mason Medical Center, and New York University Hospital, chloroprocaine has been used for spinal anesthesia for the past 5-10 years. However, 2-chloroprocaine use in spinal anesthesia has had a controversial past. In the 1980's, devastating neurologic deficits have been reported on inadvertent subarachnoid injection of epidural doses of CP, leading the FDA to not approve its use as a spinal anesthetic. It was hypothesized the preservatives (bisulphite and EDTA) and/or excessive dosage were responsible for the neurotoxicity of CP. Newer formulations have been made in early 2000's, which are preservative-free and have recently been approved for spinal use in Europe since 2012. To keep FDA antiquated policies in perspective, isobaric mepivacaine, which we have been using at HSS for over 20 years, is still not approved for spinal use.

Since its approval for use in Europe, there have been a resurgence in the number of chloroprocaine studies. Recent studies - (volunteer, retrospective and prospective) have verified the safety and efficacy of preservative-free CP, especially for ambulatory surgeries. According to clinicaltrials.gov, there are 11 registered studies using chloroprocaine spinals, two of which are in the US (Vanderbilt, Columbia). We are currently conducting a retrospective study, in collaboration with NYU Hospital/Hospital for Joint Disease, to confirm that the use of this local anesthetic is safe, and efficacious, especially since it is being used in an off-label manner. Our preliminary review has validated that chloroprocaine spinal anesthesia at these two institutions were safe and effective in providing surgical anesthesia. After examining 452 charts at HSS, we have found no incidence of TNS, which is significantly less than mepivacaine (6.4-7.4%), with no incidence of neuropraxia and urinary

retention. We believe chloroprocaine is not only safe to be used but is also the ideal spinal anesthetic to use for short procedures.

There have been studies comparing the most efficient and safe methods of facilitating earlier discharge, comparing general with different spinal local anesthetics. Studies have touted the quicker recovery from general anesthesia, but none were compared to the use of a short spinal anesthetic like chloroprocaine. This prospective study will be the first to compare general anesthesia with chloroprocaine and mepivacaine spinals (our current institution standard) after ambulatory knee arthroscopic surgeries. Our primary outcome will be time to reach PACU discharge criteria. We believe the chloroprocaine spinal will be superior to both general anesthesia and the mepivacaine spinal in sending the patients earlier from the PACU.

2.0 PRODUCT DESCRIPTION

Chloroprocaine has been approved as a spinal anesthetic in Europe since 2012 and several institutions have adopted chloroprocaine as a safer spinal anesthetic alternative in the United States.

3.0 OBJECTIVE OF CLINICAL STUDY

Outpatient knee surgeries with duration of less than one hour poses a challenge to the use of spinal anesthesia given that traditional agents remain in effect for 2-3 hours, thus creating a mismatch between length of surgery and anesthetic resolution. Spinal mepivacaine is mostly used at our institution for these surgeries but the prolonged duration of the block in the PACU impedes earlier discharge. Patients do not like prolonged PACU stays due to slow recovery from spinal anesthesia. Many centers instead use general Anesthesia (GA). While GA has the advantage of less surgery/anesthesia time ratio mismatch, the adverse effects of nausea, vomiting, prolonged emergence and pain control may contribute to lengthen discharge. Approved for spinal use in Europe in 2012, chloroprocaine is proven to be an effective local anesthetic with the advantage of faster block resolution, averaging 60 to 90 minutes. The intervention we are studying is whether chloroprocaine is a superior alternative to mepivacaine and general anesthesia in providing surgical anesthesia. We hypothesize that the use of chloroprocaine can combine the benefits of a short spinal anesthetic while avoiding the side effects of a general anesthetic, thus promoting earlier discharge.

4.0 STUDY HYPOTHESES

Outpatient knee surgery patients receiving chloroprocaine spinal anesthesia will be ready for PACU discharge earlier than patients receiving mepivacaine spinal anesthesia or general anesthesia.

5.0 STUDY DESIGN

5.1 Study Duration

Total duration of subject participation will be one week. The total duration of the study is expected to be 9 months.

5.2 Endpoints

5.2.1 Primary Endpoint

- Time until ready for discharge, defined as duration from the PACU arrival to the time the patient has reached PADSS discharge criteria.

5.2.2 Secondary Endpoints

- Induction time (from time out to induction end)
- Time of emergence (from “end of procedure time” to “room out time”)
- Time of resolution of spinal (defined as time of intrathecal injection to full resolution of motor and sensory): Motor resolution will be measured using the modified bromage score (0= able to move hips, knees and ankles; 1= able to move two of three; 2= able to move only one of three; 3= no movement); Sensory will be measured using perceived touch of normal sensation on lateral aspect of the foot (considered to be S1). RA will assess every 15 minutes until resolution starting at PACU arrival.
- Time of ambulation (defined as time of intrathecal injection to ambulation)
- Time of micturition (defined as time of intrathecal injection to micturition)
- Incidence of urinary retention (requiring urinary catheterization)
- Incidence of transient neurologic symptoms (defined as unilateral or bilateral back and buttock pain radiating to the legs) (RA phone call on POD 1 and POD 3)
- Incidence of neurologic deficits/neuropraxia (not related to operative site or surgery) (RA phone call on POD 1 and POD 3)
- Incidence of side effects related to spinal anesthesia (hypotension, bradycardia, urinary retention) (intraop and postop) [Hypotension defined as <30% SBP, bradycardia defined as HR <45)
- Incidence of block failure (measured by conversion to GA). Time of GA conversion (beginning of case or after one hour)
- Incidence of opioid related side effects (nausea, sedation, pruritus)
- Incidence of PDPH (defined as positional headache, relieved when laying flat)
- Incidence of emergence delirium /delayed emergence (defined as longer than 30 minutes from procedure end to extubation)
- Incidence of sore throat
- Incidence of drowsiness
- Incidence of PONV
- NRS Pain Scores: NRS questionnaire (Pre-op, PACU, POD 1, POD3)
    - NRS pain in PACU (at rest and activity, measured every 15 minutes)

  - Worst and average pain in PACU asked at PACU discharge
  - Current NRS pain in PACU 3 hours post PACU arrival if patient is not yet discharged
- Opioid consumption (total amount in PACU, total amount intraop, number of patients requiring IV rescue analgesia for NRS >7, POD1, POD 3)
- Time of discharge PACU (actual)
- Time of meeting discharge criteria (PADSS checklist will be made, RA will assess every 15 minutes)
- Patient Satisfaction (PACU discharge) with intraoperative anesthesia and pain control (Scale of 0 to 10, 0 being very dissatisfied, 10 being extremely satisfied)
- ORSDS (PACU discharge)
- Length of PACU stay
- Length of operative time (from incision to wound closure: from Epic)
- QoR-15 (quality of recovery score questionnaires) (Pre-op, POD 1, POD 3, and POD 7 via phone)

5.3 Study Sites

This study will take place at the main campus of the Hospital for Special Surgery.

6.0 STUDY POPULATION

6.1 Number of Subjects

The maximum number of subjects we plan to enroll in this study is 132.

6.2 Inclusion Criteria

Subjects of either gender will be included if they:

1. Written informed consent obtained from subject and ability for subject to comply with the requirements of the study.
2. Subjects scheduled for knee arthroscopy that is anticipated to be less than one hour
3. Age 18 to 80 years
4. Ability to follow study protocol
5. English speaking (secondary outcomes include questionnaires validated in English only)

6.3 Exclusion Criteria

Subjects will be excluded from the study if they:

1. Younger than 18 years old or older than 80 years old
2. Allergy or intolerance to one of the study medications

3. Chronic gabapentin/pregablin use (regular use for longer than 3 months)
4. Chronic opioid use (taking opioids for longer than 3 months)
5. Patient unable to undergo a spinal anesthetic due to any of the following:
    a. Lack of patient cooperation
    b. Difficulties with positioning
    c. Increased intracranial pressure
    d. Hypovalemia
    e. Indeterminate neurologic disease
    f. Coagulopathy
    g. Anticoagulant status
    h. Infection at the site of the needle insertion
    i. Severe spinal deformity
6. Patient unable to undergo LMA/GA due to any of the following:
    a. Inability to open mouth
    b. Complete upper airway obstruction
    c. Increased risk of aspiration: patients who have not fasted before
    d. administration of anesthesia, upper gastrointestinal bleed
    e. Suspected or known abnormalities in supraglottic anatomy
    f. Need for high airway pressures
7. Patient refusal to spinal anesthesia or LMA/GA
8. Subjects who are pregnant or breastfeeding. All female subjects of reproductive potential must have a negative pregnancy test
9. Non-English speakers

6.4 Randomization

A total of 132 subjects will be randomly assigned to one of the three groups (preservative-free 2-chloroprocaine, Mepivacaine, GA/LMA) in a 1:1:1 ratio. The randomization schedule is created using Statistical Analysis System (SAS) software by a member of the Healthcare Research Institute not otherwise involved in the trial. After entry into the study, the pharmacist will provide the medication that will be used for the study. The randomization schedule will be created up IRB approval and prior to start of study enrollment. A computer-generated randomization table will be generated by a statistician. Randomization will be carried out by the pharmacist who will provide the medication to the research team. The Anesthesiology Research Administrators will ensure that the randomization is carried out. The research assistant and patient will be blinded to which group the study patient is in.

7.0 PROCEDURES

7.1 Surgical Procedure

Pre-operatively:

After obtaining consent, baseline measurements will be taken and the subject will be randomized to a treatment group. Demographic information, QoR-15 (quality of recovery

score questionnaire), and current NRS scores at rest and with movement will be documented. Research assistant and subjects will be blinded from treatment.

Intra-op:
All groups may be given 5mg midazolam, ondansetron 4mg, ketorolac 30mg, famotidine 20mg, and dexamethasone 4mg. Propofol will be administered intraoperatively as outlined below. Subject will be monitored intra-operatively according to American Society of Anesthesiologists Standards for Basic Anesthetic Monitoring. The spinal injection and the surgical procedure will be performed in a setting with immediate availability of emergency medications and equipment for treating cardiovascular and respiratory adverse events. Intra-op opioid consumption will be documented. IV Tylenol will be ordered at end of case or PACU arrival.

Post-op: If not ordered/administered intra-op, IV Tylenol will be ordered while in PACU. The following post-operative analgesia may be ordered: Tramadol 50 mg; Tramadol 100 mg; Oxycodone 5 mg for break through pain; IV rescue hydromorphone 0.5 mg x2 q5 min (1 mg total) for NRS pain >7. The following post-operative anti-emetics may be ordered: Metoclopramide 10 mg PRN; Scopolamine patch PRN (if all IV anti-emetics fail).

PACU Visit:
Following surgery, subjects will be assessed in the PACU (1-2 hours after induction). The following information will be collected:

- Post anesthesia Discharge Scoring System (PADSS) criteria (assessed by RA every 15 minutes until criteria are met)
- Anesthesia intra-operative notes collected by non-blinded RA
- Current NRS score at rest and with movement every 15 minutes starting at PACU arrival until patient reaches PADSS discharge criteria, and once 3 post PACU arrival if patient has not yet been discharged
- Average NRS score with movement and at rest while in the PACU (asked at PACU discharge)
- Worst NRS score while in the PACU (asked at PACU discharge)
- Opioid consumption
- Opioid Related Symptom Distress Scale (ORSDS) survey
- Time of emergence (from "end of procedure time" to "room out time")
- Time of spinal resolution (defined as time of intrathecal injection to full resolution of motor and sensory) (motor measured using the modified bromage score: 0 = able to move hips, knees, and ankles, 1=able to move two of three, 2= able to move only one of three, 3= no movement. Sensory measured using perceived touch of normal sensation on lateral aspect of the foot (considered to be S1), RA to assess every 15 minute until resolution.
- Time of PACU arrival
- Time of ambulation (defined as time of intrathecal injection until time of first ambulation)
- Time of micturition (Defined as time of intrathecal injection until time of first micturition)
- Time of PACU discharge (actual, documented in EPIC)
- Time of PACU stay (PACU arrival until PACU discharge)
- Incidence of urinary retention, transient neurologic symptoms (TNS), side effects (nausea, drowsiness, puritis), post-operative dural puncture headache (PDPH),

emergence delirium/delayed emergence, sore throat, drowsiness and postoperative nausea and vomiting (PONV)

- RA will ask subjects: "Do you have any back or buttock pain that is radiating to one or both legs? Do you have a headache that gets worse when you sit up or stand?" If subject responds 'yes' to either of these questions, the RA will notify the PI and attending anesthesiologist who administered the spinal anesthetic (as is standard nursing protocol for positive findings on their POD 1 phone calls)
- Incidence of hypotension and bradycardia:
    - Hypotension defined as blood pressure <30% SBP
    - Bradycardia defined as heart rate <45 bpm

Subjects will likely be discharged on the day of surgery. Subsequent visits will occur via phone or electronically.

7.1.1 Investigational Product Application

Group 1- Preservative-free 2% Chloroprocaine(2CP) spinal group:
Subject will receive an initial bolus of intravenous propofol (0.1-0.15 mg/kg) titrated to desired clinical effect. While monitoring cardio respiratory function, propofol will be administered as a slow infusion for maintenance of anesthesia at a rate of 25-50 mcg/kg/min. Intermittent boluses of 10-20 mg to titrate to the desired sedation level at the anesthesiologist's discretion. A spinal anesthetic with preservative-free 2% chloroprocaine (2cc or 40 mg) will be performed.

Group 2- 1.5% Mepivacaine spinal group:
Subject will receive an initial bolus of intravenous propofol (0.1-0.15 mg/kg) titrated to desired clinical effect. While monitoring cardio respiratory function propofol will be administered as a slow infusion for maintenance of anesthesia at a rate of 25-50 mcg/kg/min. Intermittent boluses of 10-20 mg to titrate to the desired sedation level at the anesthesiologist's discretion. A spinal anesthetic with 1.5% Mepivacaine (3cc or 45 mg) will be performed.

Group 3- General Anesthesia:
Subject will receive an initial bolus of intravenous propofol (1.5-2.5 mg/kg) for anesthesia induction. Subsequently a laryngeal mask airway (LMA) will placed. Anesthesia will be maintained using propofol infusion (100-200 mcg/kg/min) and fentanyl (given at 25 mcg increments at a total of 200 mcg) at the discretion of the anesthesiologist. Additionally, intermittent boluses will be given in increments of 25-50 mg when changes in vital signs indicate a response to surgical stimulation or light anesthesia. No inhalation agents or nitrous will be used.

7.2 Data Collection

The following data will be collected (sources include Epic, medical records, and patient):

Pre-operative/Baseline

- DOB

- Race
- Gender
- Name
- Current NRS Pain Scores at rest and with movement
- QoR-15

Surgical procedure/Intra-Op

- Opioid consumption
- Date of surgery
- Type of surgery

PACU

- Opioid consumption
- Incidence of back pain
- Average NRS Pain Scores at rest and with movement
- Worse NRS pain score while in PACU

POD 0

- Current NRS Pain Scores at rest and with movement
- ORSDS
- Blinding assessment
- Patient satisfaction
- Induction time (time out to induction end)
- Time of emergence (“end of procedure time” to “room out time”)
- Time of spinal resolution (Motor/sensory exam)
- Time of ambulation
- Time of micturition
- Incidence of urinary retention
- Incidence of TNS
- Incidence of neurological deficits/neuropraxia
- Incidence of side effects
- Incidence of PDPH
- Incidence of emergence delirium/delayed emergence
- Incidence of sore throat
- Incidence of drowsiness
- Incidence of PONV
- Time of discharge
- Time of meeting discharge criteria
- Time of PACU arrival

POD 1

- Current NRS Pain Scores at rest and with movement
- Opioid consumption
- ORSDS
- Incidence of TNS
- Incidence of neurological deficits/neuropraxia
- Incidence of PDPH

- Incidence of back pain
- Qor-15 (phone)
- Average NRS score at rest and with movement

POD 3

- Current NRS Pain Scores at rest and with movement
- Opioid consumption
- Incidence of TNS
- Incidence of neurological deficits/neuropraxia
- Incidence of PDPH
- Incidence of back pain
- QoR-15 (phone)
- Average NRS score at rest and with movement

POD 7

- QoR-15 (phone)

7.3 Schedule of Assessments

Procedures	Pre-Op	Surgery	6 Weeks ± 2 weeks	12 Weeks ± 2 weeks	6 Months ± 4 weeks	1 Year ± 8 Weeks	2 Years ± 8 Weeks	Revision Surgery**
Informed Consent & Eligibility Review	X							
Randomization	X							
History	SOC		SOC	SOC	SOC	SOC	SOC	SOC
Physical Exam	SOC		SOC	SOC	SOC	SOC	SOC	SOC
Routine X-rays	SOC		SOC	SOC	SOC	SOC	SOC	
Lumbar MRI	SOC			X*				
Routine Lumbar CT Scan	SOC							
Patient-reported Outcomes	SOC		SOC	SOC	SOC	SOC	SOC	SOC
Pain Medication Assessment	SOC	SOC	SOC	SOC	SOC	SOC	SOC	SOC
Work and Functional Assessment	SOC	SOC	SOC	SOC	SOC	SOC	SOC	SOC
Adverse Event Assessment		X	X	X	X	X	X	X
Ease of Dissection Scoring								X
Histological Analysis Scoring								X

* = First 20 subjects (5 in each treatment arm) enrolled as part of study pilot group
**=Patient will be re-evaluated by the investigator as per standard follow-up post-operatively at a minimum interval of 6 weeks and 12 weeks post-operatively

8.0 STATISTICAL ANALYSIS

The primary outcome (time until ready for PACU discharge) will be compared between the chloroprocaine, mepivacaine, and general anesthesia groups with three pairwise two-sample t-tests or Wilcoxon rank-sum tests, depending upon the distribution of the data. Effect size will be presented as difference in means or Wilcoxon-Mann-Whitney odds with 95% confidence intervals. Continuous secondary outcomes measured at a single time point will be analyzed in the same manner as the primary outcome. Categorical secondary outcomes measured at a single time point will be compared between groups using $\chi 2$ or Fisher's exact tests, with effect sizes presented as risk differences and relative risks with 95% confidence intervals. Outcomes measured at multiple time points will be analyzed using regression based on a generalized estimating equations (GEE) approach. A treatment by time interaction term will be included in all GEE models regardless of corresponding P value.

Balance on demographics and baseline characteristics will be assessed by calculating standardized differences (difference in means or proportions divided by the pooled standard deviation) between groups. Balance will be assessed using two thresholds: (1) 1.96 x (2/44)1/2 = 0.42 and (2) 0.2 (Austin 2009). All analyses will be performed on an intention-to-treat basis.

References
(1) Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009; 28: 3083-107.

9.0 ADVERSE EVENT ASSESSMENT

All Adverse Events (AEs) will be reported in the final study report. Definitions for Adverse Event (AE) used in this study are listed below and are based on FDA and international guidelines:

9.1 Adverse Event (AE)

Any untoward or unfavorable medical occurrence in a participant, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participant's participation in the research, whether or not considered related to the participant's participation in the research.

9.2 Serious Adverse Events (SAE)

Adverse events that result in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

9.3 Adverse Event Reporting

Any adverse event(s) or deviation(s) from this protocol will be brought to the attention of the PI, and will be recorded and reported to the IRB.

10.0 INVESTIGATOR RESPONSIBILITIES, RECORD AND REPORTS

10.1 Subject Consent and Information

Potential subjects will be screened prior to day of scheduled surgery based on inclusion and exclusion criteria reviewed in the subject's medical record. After discussion of the study with the surgeon, eligible subjects will be approached on the day of surgery prior to surgery and invited to participate in the study. Informed consent will be obtained from all subjects before conduct of any study-related procedures.

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