# Intraoperative Acupuncture for Low-Dose Opioid Total Knee Replacement: An Observational Prospective Cohort Study

FUNDER: Department of Anesthesiology

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# PROTOCOL SYNOPSIS

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| **Protocol Title:** | Intraoperative Acupuncture for Low-Dose Opioid Total Knee Replacement: An Observational Prospective Cohort Study |
| **Protocol Number:** | 2019-1193 |
| **Protocol Date:** | 03/08/2021 |
| **Sponsor:** | Department of Anesthesiology |
| **Principal Investigator:** | Stephanie Cheng, MD |
| **Objective:** | We will investigate the feasibility of maintaining a low-dose opioid regimen after total knee replacement (TKR) through a standardized perioperative analgesic protocol including intraoperative auricular acupuncture. |
| **Study Design:** | Prospective Cohort Study |
| **Enrollment:** | 41 |
| **Subject Criteria:** | 1. ASA of 1 or 2<br>2. Age 18-80<br>3. Undergoing a primary total knee replacement<br>Desire to attempt a low opioid or opioid free pathway |
| **Data Collection:** | Sources: EPIC, Medical Records, and Patient Reported.<br>Variables: Name, DOB, Race, Gender, Experience with Acupuncture, Tourniquet Time, NRS Pain scores at Rest, Opioid Consumption, Patient Satisfaction, ORSDS, Medical Marijuana Usage, Non-Pharmacological Pain Relief, Headache, Range of Motion, Nerve Block Success. |
| **Statistical Analysis:** | • One-sample test of proportions (Z-test)<br>• Alpha level: 0.025 (one-sided)<br>• Beta or power level: 90% |

## 1.0 INTRODUCTION

In the setting of the opioid abuse epidemic, it has become even more important for anesthesiologists to seek alternative analgesics to treat perioperative pain. The use of peripheral nerve blocks and oral non-narcotic analgesics have helped reduce opioid consumption after total knee replacement (TKR), but a highly successful low-dose opioid regimen, with the goal of being opioid free, for total knee replacements has not been achieved. Intraoperative auricular acupuncture may be a low-cost adjunctive therapy to assist in achieving a minimal opioid perioperative experience following TKR.

In recent years, opioid abuse has skyrocketed in the United States, with more than 11 million people misusing prescription opioids in 2016, including 2 million people abusing narcotics for the first time[1]. A recent report using data from the National Survey on Drug Use and Health from 2009-2014 found that older adults who abuse narcotics are more likely to obtain them legally from their physicians[2], including 40% of patients aged 50-64 and almost 50% of those over 65. Frequently, these patients are first exposed to opioids during their perioperative course. One recent study reported 6% of opioid-naive patients became chronic users at 90 days after surgery[3]. Additionally, the Intraoperative use of opioids can lead to acute opioid tolerance and hyperalgesia that causes patients to require additional opioids postoperatively[4,5].

With increasing use of regional anesthesia and non-opioid analgesics, the potential for "opioid-sparing" anesthesia has been considered and described by various case reports[6-8] randomized trials[5,9]. In addition to non-opioid analgesics, Auricular therapy has been studied as a method for relieving perioperative pain in a wide range of surgeries including IVF[10], GI[11], ENT[12], and orthopedic procedures. In a 2014 meta-analyses of 13 RCTs with 806 subjects, a mean decrease in pain from auricular therapy was 1.59 standard deviations greater than that seen in the sham therapy group[13]. Looking at studies focusing on orthopedic procedures, several positive reports of auricular therapy exist in the literature. In 2005, Usichenko and colleagues reported on their pilot work using semi-permanent auricular needles for perioperative pain management of patients undergoing knee arthroscopy and total hip arthroplasty demonstrating reductions in postoperative analgesic requirements[14-16].

Regional anesthesia and use of multimodal analgesia are well-known strategies for reducing opioid consumption after total joint replacement surgery. This study looks to extend the use of auricular therapy as part of a low opioid or opioid-sparing anesthetic regime for total knee replacements, and assist in achieving a low dose opioid maintenance perioperative course following the procedure.

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## 2.0 OBJECTIVE(S) OF CLINICAL STUDY

The feasibility of an opioid-minimizing protocol that incorporates acupuncture for postoperative analgesia is unknown for patients undergoing total joint replacement. Furthermore, previous studies of acupuncture as an adjunctive therapy for postoperative analgesia have primarily investigated patient satisfaction rather than the impact on postoperative opioid consumption. The majority of studies also place acupuncture needles preoperatively, rather than following induction of anesthesia. We hope to show that placing auricular therapy needles intraoperatively is a feasible part of a protocol for motivated patients to minimize opioids after total knee arthroplasty.

The majority of patients undergoing total knee replacement rely on opioids for postoperative analgesia. These medications have undesirable side effects and potential for abuse and addiction. The aim of this cohort study is to determine the incidence rate of patients who are able to maintain a low dose opioid regimen after TKR with the use of a multimodal approach that includes intraoperative auricular acupuncture protocol.

1. Maintain a low dose opioid regimen (15 pills or less of 5mg oxycodones or 112.5 OME) from POD 0 to POD 30 throughout their TKR.
2. What are the NRS pain scores (numeric scale 0-10) assessed in the PACU at spinal resolution. Additional pain score assessments will be performed on postoperative days 1-3 (approximately 24, 48, 72 hours postoperatively), postoperative day 14 (the first postoperative clinic visit) and postoperative day 30.
3. What is the incidence of deviations from the intraoperative and postoperative pain regimen protocol, and what are those deviations?
4. For those who exceed the low dose regimen, how many oxycodone (5mg) pills are used by these patients (as measured at each of the time points described in question 2?
5. How many patients require rescue intravenous narcotic?

Secondary aims of the study are to assess patient satisfaction with their overall perioperative pain control and the experience of the intraoperative auricular acupuncture in particular, and to determine the incidence of adverse events commonly associated with opioid use, specifically nausea, vomiting, pruritus, and constipation.

1. How satisfied are patients with their overall perioperative pain control?
2. How satisfied are patients with their experience with the auricular acupuncture?
3. What is the incidence of each of the following: nausea, vomiting, pruritus, and constipation?

## 3.0 STUDY HYPOTHESES

This is a prospective cohort study to assess the feasibility of patients to undergo TKR while adhering to a low-dose opioid regimen by using a multimodal analgesic approach that includes intraoperative auricular acupuncture. We hypothesize that it will be feasible to maintain a low-dose opioid regimen during TKR while following the intraoperative auricular acupuncture protocol, and that patients will be satisfied with their pain control with a low incidence of adverse events.

## 4.0 STUDY DESIGN

### 4.1 Endpoints

#### 4.1.1 Primary Endpoint

- The primary outcome is the incidence of patients who maintain a low-dose opioid regimen (15 pills or less of 5mg oxycodone or 112.5 OME) from POD 0 to POD 30 throughout their TKR.

#### 4.1.2 Secondary Endpoints

- Total opioid consumption (PACU, POD1, POD7, POD14, POD30)
- NRS pain scores at rest and with movement (PACU, POD1, POD7, POD14, POD30)
- Satisfaction with postoperative analgesia POD1
- Satisfaction with intraoperative auricular acupuncture POD1
- Satisfaction with the whole protocol POD 30
- Deviation from prescribed oral pain regimen including need for rescue medications POD 30
- Incidence of nausea, vomiting, pruritus, constipation (PACU, POD1)
- Postoperative range of motion (extension and flexion, measured at 6 week surgeon office visit)
- Tourniquet time (Intra-op)

### 4.2 Study Sites

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

## 5.0 STUDY POPULATION

### 5.1 Number of Subjects

41

### 5.2 Inclusion Criteria

Subjects of either gender will be included if:

1. ASA of 1 or 2
2. Age 18-80
3. Undergoing a primary total knee replacement
4. Desire to attempt a low opioid or opioid free pathway

### 5.3 Exclusion Criteria

Subjects will be excluded from the study if:

- Non-English speaking
- Patients with the inability to understand or follow study protocol
- Opioid use in the last 6 weeks or chronic pain patient
- Cannot receive neuraxial anesthesia and/or peripheral nerve block
- Patients with contraindications to intra-op protocol (e.g., patient cannot take acetaminophen or ketorolac due to liver or kidney disease)
- Patients with implanted cardiac device such as a pacemaker or AICD
- Active ear infection
- Non-native ear, previous scarring or surgical manipulation of ear
- Patients with gauges or other deforming ear piercing (small non-deforming ear piercings are ok) present in ears
- Allergy to nickel

## 6.0 PROCEDURES

### 6.1 Intraoperative Protocol

Following patient transfer to the operating room, neuraxial anesthesia (spinal or combined spinal epidural (CSE) with up to 4cc mepivacaine 1.5%) and two blocks for postoperative pain (IPACK and adductor canal peripheral nerve blocks) will be placed by the anesthesiologist. Each peripheral nerve block will be dosed with 15cc bupivacaine 0.5% with 2mg preservative free dexamethasone (30cc total). Sedation will be provided intraoperatively with midazolam (up to 5mg), ketamine (up to 50mg), ketorolac (up to 30mg), and propofol (titrated to effect). Tranexemic acid (TXA) will be dosed per surgeon request.

Once sedation has been deemed adequate by the anesthesiologist, a certified medical acupuncturist will perform ipsilateral Auricular Trauma Protocol (ATP) acupuncture at eight

ear points (Hypothalamus, Amygdala, Hippocampus, Prefrontal Cortex, Point Zero, Shen Men, Insula, Vagus) with 30Hz electrostimulation at two of those points (Shen Men and Hypothalamus). Acupuncture needles will be left in place and stimulated for 60 min and then removed. If an epidural is placed, it may be re-dosed with lidocaine as needed (up to 100mg total) and will be removed prior to transfer to the recovery room.

A periarticular injection (PAI) will be placed by the surgeon during the surgery (timing at the discretion of the surgeon) and will include:

- 30cc 0.5% bupivacaine with 1:100,000 Epi
- 40mg of depomedrol (1cc)
- 500mg cefazolin (10cc)
- 20cc of 0.9% NaCl solution

Postoperatively, all patients will receive oral dexamethasone 10mg every 8 hours (3 doses), intravenous ketorolac 15mg (7.5 if under 50kg) every 6 hours, and oral acetaminophen 1000mg every 6 hours until discharged. For pain not controlled on this regimen, patients will be offered oral oxycodone, and intractable pain will be treated at the discretion of the provider. After 24 hours, patients will be transitioned to and discharged on oral meloxicam 7.5mg every 6 hours and oral acetaminophen 1000mg every 6 hours for thirty days. The PA or fellow working with the surgeon will place a discharge order for 42 oxycodone 5mg with no refills. Patients will be discharged with Mobic 15mg (7.5 if under 50kg) and acetaminophen 500mg.

NRS pain scores (numeric scale 0-10) will be assessed at spinal resolution in the PACU. postoperative admission. Additional pain score assessments will be performed on postoperative days 1, postoperative day 14 (the first postoperative clinic visit) and postoperative day 30. In addition, at each of those times, the number of oxycodone pills used (5mg each) or the MME, any deviations from the standing oral pain medication regimen (e.g., early discontinuation of ketorolac or acetaminophen), and any adverse events (e.g., postoperative nausea or vomiting, bleeding, pruritus) will be assessed.

### 6.2 Data Collection

The following data will be collected:

**Pre-operative/Baseline**

- basic demographic data
- patient weight & height, BMI
- experience with acupuncture
- NRS scores at rest
- Medical marijuana usage

**Surgical procedure (Intra-operative)**

- date of surgery
- type of surgery
- tourniquet time
- nerve block success

**Post-Operative Day 0 (POD 0)**

- NRS pain scores at rest
- Opioid consumption
- ORSDS

**Post-Operative Day 1 (POD 1)**

- NRS pain scores at rest
- Opioid consumption
- Patient satisfaction
- ORSDS
- Non-pharmacological pain relief
- Headache

**Post-Operative Day 7 (POD 7)**

- NRS pain scores at rest
- Opioid consumption

**Post-Operative Day 14 (POD 14)**

- NRS pain scores at rest
- Opioid consumption

**Post-Operative Day 30 (POD 30)**

- NRS pain scores at rest
- Opioid consumption
- Patient satisfaction
- Medical marijuana usage
- Non-pharmacological pain relief

**6 Weeks Post-Operative**

- Range of motion

## 7.0 STATISTICAL ANALYSIS

- Proposed analysis: One-sample test of proportions (Z-test)
- Interim analysis planned: No
- Alpha level: 0.025 (one-sided)
- Beta or power level: 90%
- Primary outcome variable estimate: Estimated percentage of patients who maintain a low-dose opioid regimen (15 pills or less of 5mg oxycodone or the OME) from POD 0 to POD 30 throughout their TKR = 27.8%
- Number of groups being compared:1
- Effect size or change expected between groups: Testing whether the percentage of patients who can maintain a low-dose opioid regimen (15 pills or less of 5mg oxycodone or the MME) from POD 0 to POD 30 throughout their TKR is higher than 9%
- Resulting number per group: 37

- Total sample size required: 37 +4 (10% attrition rate)= 41

Proportion (27.8%) comes from practice data by one anesthesiologist who also practices medical acupuncture (Dr. Stephanie Cheng) and one surgeon (Dr. Michael Ast) on patients undergoing TKR from October to December 2018.

Null proportion (9%) comes from unpublished study (PI: Dr Todd Albert, 2018, "Opioid consumption and disposal patterns after total knee arthroplasty as characterized by a novel mobile phone text messaging platform."). The purpose of getting the null proportion is to see what percentage of patients can maintain a minimal opioid consumption after TKR without a controlled multimodal analgesic approach that includes intraoperative auricular therapy.

Primary outcome: the percentage of patients who can maintain a low-dose opioid regimen (15 pills or less of 5mg oxycodone or the OME) from POD 0 to POD 30 throughout their TKR will be compared to 9% using a one-sample test of proportion (Z-test).

Secondary outcomes (listed above) measured once per patient will be analyzed by t-test or Wilcoxon rank-sum test (continuous data) and $\chi 2$ or Fisher's exact test (categorical data). Outcomes measured multiple times per patient will be analyzed using regression based on a generalized estimating equation approach.

## 8.0 ADVERSE EVENT ASSESSMENT

All Adverse Events (AEs) will be reported in the final study report.