# Impact of volume of local anesthetic injected for adductor canal block on recovery profile and block characteristics following total knee arthroplasty.

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**Adductor Canal for TKA Protocol**

Impact of volume of local anesthetic injected for adductor canal block on recovery profile and block characteristics following total knee arthroplasty.

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## Investigator's Agreement

1. I have read this protocol and agree to conduct this trial in accordance with Good Clinical Practice (GCP), all stipulations of the protocol, the Declaration of Helsinki, and applicable regulatory requirements as stated by my human subjects testing oversight body [e.g., independent ethics committee (IEC) or institutional review board (IRB)].

2. I will personally conduct or supervise the described investigation(s). This includes informing all associates, colleagues, and employees assisting in the conduct of the study about their obligations in meeting the above commitments.

3. I agree to maintain the confidentiality of all information received or developed in connection with this protocol.

4. I agree that all electronic signatures will be considered the equivalent of a handwritten signature and will be legally binding.

Protocol Title: Impact of volume of local anesthetic injected for adductor canal block on recovery profile and block characteristics following total knee arthroplasty.

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Signature of Principal Investigator — Date

Kristopher Schroeder, MD

Name of Principal Investigator (printed or typed)

## Summary

Total knee arthroplasty (TKA) can be associated with a large amount of postoperative pain. This pain can oftentimes be severe enough to limit participation in physical therapy and ultimately delay discharge resulting in increased cost. Several strategies have been developed in an effort to decrease postoperative pain following TKA while maintaining lower extremity strength and maximizing participation in physical therapy. Recently, adductor canal blockade has gained popularity as it is reported to provide analgesia to the anterior knee without resulting in significant quadriceps muscle weakness. However, few studies have carefully evaluated the impact of volume of injection of local anesthetic into the adductor canal on motor weakness or pain control. The ability to achieve similar pain control with decreased volumes of local anesthetic would allow the surgery team to apply more local anesthetic to posterior knee structures. Decreased volumes of local anesthetic may also be associated with a decreased risk of local anesthetic toxicity. This study aims to carefully evaluate this relationship using a physical therapy evaluation method that relies on both motor strength and pain control. In addition, we hope to carefully evaluate motor strength using a novel method of strength measurement in an effort to further evaluate the impact of volume of injection of local anesthetic into the adductor canal on motor strength.

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## Schedule of activities

| | Screening Visit 1 | Procedure Visit 2 | Post-Adductor Block Visit 3 | PACU Visit 4 | 24-hours Post-op Visit 5 | 48-hours Post-op Visit 6 |
|---|---|---|---|---|---|---|
| Window | Up to 60 days before surgery | Morning of Surgery | 15 minutes after adductor block placed +/- 10 mins | Following surgical procedure | 24 hours post-op +/- 6 hours | 48 hours post-op +/- 6 hours |
| Screening and Eligibility | X | X | | | | |
| Informed Consent | X | X | | | | |
| Demographics | X | X | | | | |
| Medical History | X | X | | | | |
| Quadricep motor strength and adductor strength assessment (Kiio sensor) | | X | X | | | |
| Sensory Leg Exam[1] | | X | X | | | |
| Questionnaires and Scores[2] | SOC | SOC | | | | |
| Pain Questionnaire[3] | | | | X | X | X |
| Physical Therapy Assessment and Walk Test[4] | | | | | X | X |
| Concomitant Medications[5] | X | X | X | X | X | X |
| Adverse Events | X | X | X | X | X | X |

[1]Temperature and Sensation will be examined using a pinprick and cold sensory technique

[2] SF12 mental component and physical component, WOMAC and Knee Society Score, UCLA activity score, range of motion (and degree of varus/valgus deformity will be collected

[3] Pain at rest, pain with activity, opioid consumption, nausea, pain disturbing sleep, location of most severe pain and satisfaction with regional anesthesia technique will be assessed

[4] Pain with physical therapy, quadriceps strength, passive flexion/extension range of motion, postoperative quadriceps strength, postoperative adductor strength, and 10 meter walk test (gait velocity) using Kiio sensor

[3] Medications that are taken at home regularly and prior to arrival on the day of surgery, surgery premedication, and all medications for nausea and pain will be recorded.

## List of abbreviations and definitions

| | |
|---|---|
| AE | Adverse event |
| CFNB | Continuous Femoral Nerve Blockade |
| CACNB | Continuous Adductor Canal Nerve Blockade |
| DSMC | Data Safety Monitoring Committee |
| PACU | Post-Anesthesia Care Unit |
| POD | Post-Operative Day |
| SAE | Serious Adverse Event |
| SSFNB | Single Shot Femoral Nerve Block |
| SSACNB | Single Shot Adductor Canal Nerve Block |
| TKA | Total Knee Arthroplasty |

## 1. Introduction

### 1.1 Background

Postoperative analgesia for total knee arthroplasty (TKA) is incredibly important as it allows for effective physical therapy and ultimately ensures proper function of the implanted joint hardware. Unfortunately, TKA is oftentimes associated with pain severe enough to limit participation in physical therapy which can ultimately result in prolonged hospitalizations and perhaps decreased joint function. A number of strategies have been reported to decrease the pain associated with TKA. Opioids are commonly utilized but they can be associated with a number of potential side effects including nausea, itching, respiratory depression, tolerance and the potential for abuse. Epidural analgesia has been utilized for postoperative analgesia but this strategy requires urinary catheterization (potential source of increased incidence of urinary tract infections), causes significant vasodilation with resulting hypotension and can cause bilateral lower extremity weakness that can undermine efforts at early physical therapy and rehabilitation. Femoral nerve blockade and femoral nerve catheters have the potential to decrease pain in the anterior knee but use of this technique is limited by incomplete analgesia and quadriceps motor weakness. Some groups have advocated for the substitution or addition of sciatic or obturator nerve blocks to femoral nerve blockade but this is at the expense of increased lower extremity weakness and little potential clinical benefit.[1-5]

In an effort to balance the need for effective postoperative analgesia with the need to maintain lower extremity muscle strength for active participation in physical therapy, a number of groups have begun to evaluate the adductor canal block. The adductor canal is located in the middle 1/3 of the thigh and includes the saphenous nerve and nerve to the vastus medialis. The primary advantage to adductor canal blockade versus femoral nerve blockade is a potential sparing of the nerves to the quadriceps muscle and therefore preservation of lower extremity motor strength.[6-8] Kwofie et al reported in a study of 16 volunteers that there was no change in quadriceps strength or hip adduction following the injection of 15 ml of local anesthetic. This is interesting as the obturator nerve is reported to travel within the adductor canal and is responsible for hip adduction. Kwofie et al also reported that SSACNB resulted in significantly decreased impairments with balance compared to a SSFNB.[9]

To this point, the majority of studies evaluating adductor canal blockade have focused on continuous techniques and little has been done to evaluate single shot techniques. Continuous techniques have the potential to extend analgesia but this is at the expense of increased cost, effort, resource utilization and potentially increased risk of infection.

The safety of CACNB technique was highlighted by a study by Henningsen et al where no cases of nerve injury related to analgesic technique were reported in a series of 97 patients.[10] Andersen et al compared a CACNB vs control in 40 patients and found that the intervention group reported decreased pain and sleep disturbances while retaining the ability to ambulate soon after surgery.[11] Mudumbai et al evaluated 180 patients undergoing TKA and discovered that continuous adductor canal nerve blockade (CACNB) relative to continuous femoral nerve blockade (CFNB) resulted in greater ability to ambulate (37 m vs 6 m) on POD 1 and similar pain scores.[8] Jaeger et al examined a similar group of 54 patients presenting for TKA and found that CACNB relative to CFNB resulted in decreased quadriceps weakness and no difference in pain, opioid consumption or weakness.[12] Jenstrup et al reported that, compared to placebo, CACNB resulted in decreased pain with flexion and opioid consumption.[13] Only recently has a study comparing SSACNB and SSFNB been published. This study demonstrated that SSACNB resulted in decreased postoperative quadriceps weakness and similar pain control to SSFNB.[14] Of interest, previous research has demonstrated that 15 ml 0.5% ropivacaine is required to produce ultrasound guided

femoral nerve blockade (including sensory and quadriceps motor weakness) but no such study has yet been done for the adductor canal block.[15] It is possible that larger volumes of local anesthetic injected into the adductor canal could result in proximal spread of local anesthetic and increase quadriceps weakness and difficulty ambulating. It is also possible that decreased volumes of injection may result in inferior pain control and difficulties participating in physical therapy.

### 1.2 Rationale and hypothesis

We propose a prospective, single-center, randomized trial to evaluate the impact of volume of injection for adductor canal block on patient recovery profile and block characteristics when performed for total knee arthroplasty.

## 2. Objectives

### 2.1 Primary outcome and endpoint

The primary purpose of this study is to compare the patient's ability to ambulate on POD 1 in patients that have received 5, 10 or 20 ml local anesthetic injection for SSACNB. This will be evaluated by determining how quickly a patient is able to ambulate over 10 meters on POD 1 (10 meter walk test).

### 2.2 Secondary outcomes and endpoints

The secondary purposes of this study are to compare the following perioperative variables:

**Pre/Intraoperative Variables**:

- Opioid consumption
- Sensory blockade
- Patient perceived discomfort with procedure
- Preoperative quadriceps strength
- Preoperative adductor strength
- SF12 mental component and physical component
- WOMAC and Knee Society Score
- UCLA activity score
- Preoperative range of motion
- Degree of varus/valgus deformity.

**PACU Variables:**

- Pain
- Opioid consumption
- Nausea
- Time in PACU (duration)
- Satisfaction with regional anesthesia
- Location of most severe pain

**Floor Variables**:

- Pain at rest
- Pain with activity
- Opioid consumption
- Nausea
- Duration of hospitalization

- Pain disturbing sleep
- Location of most severe pain
- Satisfaction with regional anesthesia

**PT Variables**:
- Pain with physical therapy
- Quadriceps strength
- Passive flexion/extension range of motion
- Postoperative quadriceps strength
- Postoperative adductor strength

## 3. Study design

This study is a prospective, single-center, randomized trial in which 60 subjects will be enrolled at the University of Wisconsin Hospitals and Clinics (UWHC). These subjects must meet study eligibility criteria and be scheduled to undergo an elective total knee arthroplasty. These subjects must also agree to undergo neuraxial anesthesia as the primary anesthetic for their surgical procedure and agree to an adductor canal block for postoperative analgesia. Patients will be randomized to receive 5, 10 or 20 mL of 0.5% bupivacaine injected into their adductor canal. Strength following the block and recovery characteristics following TKA will then be evaluated including pain, strength and ability to participate in physical therapy.

## 4. Study population

### 4.1 Inclusion criteria

Each patient must meet all of the following inclusion criteria to be enrolled in the study.

1) The subject is scheduled for elective unilateral TKA
2) The subject is ≥ 18 years and ≤ 80 years;
3) The subject's weight is between 70-120 kg; and
4) The subject's primary anesthesia care team has planned for a neuraxial anesthetic (i.e. spinal, epidural or combined-spinal epidural).
5) The patient agrees to receive an adductor canal block.
6) American Society of Anesthesiologists class 1-3

### 4.2 Exclusion criteria

Patients meeting any of the following exclusion criteria are not to be enrolled in the study.

1) Subject is < 18 years of age or >80 years of age;
2) Subject is non-English speaking;
3) Subject is known or believed to be pregnant;
4) Subject is a prisoner;
5) Subject has impaired decision-making capacity; per discretion of the Investigator
6) Symptomatic untreated gastroesophageal reflux or otherwise at risk for perioperative aspiration;
7) Any condition for which the primary anesthesia care team deems neuraxial anesthesia inappropriate;
8) Significant pre-existing neuropathy on the operative limb;

9) Significant renal, cardiac or hepatic disease per discretion of the investigator.
10) American Society of Anesthesiologists class 4-5
11) Known hypersensitivity and/or allergies to local anesthetics
12) Chronic Opioid Use (daily or almost daily use of opioids for > 3 months)

### 4.3 Protected populations

***Prisoners***

Due to the complexity of state and federal requirements governing the participation of prisoners in research, patients who are prisoners will not be considered for participation in this trial. In the unlikely event that a subject becomes a prisoner while participating in this trial, study procedures will stop and the subject will be returned to the clinical mode used prior to the intervention period or, if desired, a ventilator mode requested by the clinical care team.

***Pregnancy***

Patients who are known to be pregnant will be excluded from participation.

## 5. Trial interventions

The intervention portion of this study is the randomized assignment (1:1:1) to receive 5, 10 or 20 ml of 0.5% bupivacaine, incrementally injected. All studied volumes are well within the acceptable range for SSACNB. Randomization will be accomplished using an online service (www.randomizer.org) and prefilling sealed envelopes determining each subject's intervention group. In all other aspects, the subject will receive the standard of anesthesia care appropriate for their surgery or procedure as determined by the primary anesthesia team caring for the subject.

### 5.1 Allocation to intervention

Randomization of the volume of bupivacaine will be determined by opening a sequential, pre-sealed envelope with the group assignment designated within. Randomization will be accomplished using an online service (www.randomizer.org).

Each study subject and the anesthesia team caring for the patient in the operating room will be blinded to the study volume the patient received; however, the anesthesia provider performing the block (separate from the provider caring for the patient in the operating room) will not be blinded to the study volume injected and will have access to all monitors deemed appropriate by the primary anesthesia team caring for the subject. PACU/floor nursing and physical therapy staff will be blinded to volume of injection. The surgery team and study member responsible for pre/postoperative data collection will also be blinded to study drug volume.

## 6. Subject recruitment and consent

### 6.1 Subject identification and Screening

The study team will review the medical records of patients scheduled for an elective TKA to check for eligibility. Those who appear eligible will receive a phone call from a study team member who is also involved in their clinical care 1-7 days prior to their surgery. We will briefly describe the study procedures and voluntary nature, and answer any questions they have about it. If the subject is interested in participation, they will be instructed to arrive 1 hour earlier than their scheduled surgery arrival time so that there is time for consenting, considering participation, and confirming eligibility of those who agree to participate. Patients scheduled for an arrival time at or before 8:00 a.m. will not eligible for the study. All protected health information used during the screening process of a potential subject will be the minimum necessary for the conduct of this study. Any protected information recorded will be destroyed at the end of the screening process.

### 6.2 Recruitment and consent

The identified patients will be given written information about the study at the time of check-in for their scheduled procedure. Once the anesthesia provider talks with the subject in order to confirm that they are a candidate for both spinal anesthesia and an adductor canal block (this conversation is standard care), a research team member will conduct the consent process in the surgery or procedure holding area. In order to ensure the candidate's privacy and confidentiality, the cubicle's curtain or room door will be closed. In a tone of voice insufficient for others to overhear the conversation and in the presence of only those immediately accompanying the patient and those who are directly involved with the patient's care, the study purpose, procedures, risks, benefits, and alternatives will then be discussed. The written information about the study provided to the candidate at the time of their check-in will be reviewed and they will be instructed to take as much time as needed to consider participation. While any study staff member may conduct the informed consent discussion and obtain informed consent, a study physician will be available at all times for any consent-related questions. Any questions that the candidate may have will be answered. Undue coercion will be prevented by stressing that the potential subject does not have to agree to participation and that the future care of the potential subject will not change regardless of the decision about participation. If the candidate has no further questions and would like to participate, they will be asked to sign the written informed consent document.

## 7. Activities and measurements

Prior to the procedure:

The subject will be met in the preoperative area by a staff anesthesiologist, who interviews and examines the subject. A full explanation of the neuraxial anesthetic and adductor canal block, including risks, benefits and alternatives, will be given and informed consent for anesthetic services obtained. Quadriceps motor strength and adductor strength will be assessed prior to any nerve blockade. Muscle strength will be assessed with the kiio Sensor (Kiio Inc., Madison, WI USA). The kiio sensor is a force monitoring device that provides objective measurements of patient strength (traditional measurements or Manual Muscle Testing typically relies on subjective assessments by medical staff). To assess the subject's quadriceps and adductor strength, the kiio sensor will be attached to the subject's ankle or upper leg and subject will be asked to forcefully extend the leg at the knee or adduct their leg. The kiio Sensor is not currently commercially available and is currently in the development stage (see attached Phase I progress report – APPENDIX D). A sensory exam of the leg (temperature and pinprick) will also

be conducted prior to nerve blockade to determine baseline sensation of femoral, obturator and lateral femoral cutaneous nerves. For these tests, the jagged edges of a broken tongue depressor and alcohol swab will be used to produce pinprick and cold sensation. Subjects will be asked to report if sensation is normal, absent or decreased to both pinprick and cold.
From the subject's medical record the SF12 mental component and physical component, WOMAC and Knee Society Score, UCLA activity score, preoperative range of motion and degree of varus/valgus deformity will be collected. These scores and procedures are standard of care for all patients undergoing a TKA.

Adductor Canal Block Procedure:
An intravenous catheter will be placed, the subject will be transported to the block room or another room appropriate for provision of regional anesthesia and the subject will be pre-medicated with midazolam and/or fentanyl as needed at the discretion of the staff anesthesiologist.

Adductor canal blockade will be performed with the assistance of ultrasound guidance following sedation with midazolam and fentanyl as deemed appropriate by the staff anesthesiologist. The adductor canal will be located in a mid-thigh position. A Stimuplex needle (B. Braun Medical Inc., Melsungen, Germany) will be inserted in-plane to the ultrasound probe until the tip of the needle is appropriately positioned.

Study Randomization:
Following negative aspiration, SSACNB volume will be randomized and subjects will receive 5, 10 or 20 ml of 0.5% bupivacaine will be incrementally injected. Randomization of the volume of bupivacaine will be determined by opening a sequential, pre-sealed envelope with the group assignment designated within. All studied volumes are well within the acceptable range for SSACNB.

15 minutes post-block placement:
A sensory examination will be done 15 minutes following adductor canal block with pin prick (sharp end of tongue depressor broken in two) and alcohol swab in distribution of femoral, obturator and lateral femoral cutaneous nerve. Motor examination of quadriceps and adductor strength will also be tested 15 minutes following adductor canal blockade.

During the Surgical Procedure:
Neuraxial anesthesia will be performed as normally accomplished prior to initiation of the surgical procedure. Generally, this involves the administration of a combined-spinal-epidural anesthesia with 2.5 – 3 ml 0.5% bupivacaine administered into the intrathecal space.

In the operating room and procedural suite, monitors will be applied to the subject per established American Society of Anesthesiology (ASA) guidelines. At a minimum, these include non-invasive monitoring of blood pressure by automated cuff, oxygen saturation via pulse oximetry, heart rate and rhythm by 3-lead continuous electrocardiographic (ECG) tracing, core body temperature and expired carbon dioxide concentration. Additional monitoring may be applied on a case-by-case basis as deemed appropriate by the attending anesthesiologist. Ongoing sedation with midazolam, fentanyl and propofol will be provided as deemed appropriate by the staff anesthesiologist.

The surgical team will inject 50 ml 0.125% bupivacaine with 30 mg ketorolac (when deemed to be clinically appropriate) into the joint and posterior knee at the conclusion of the surgical procedure.

Post-Procedure:
The patient will be visited in the PACU to assess pain, opioid consumption, nausea, duration of PACU stay, satisfaction with regional anesthesia technique and location of most severe pain. This information will be ascertained by questioning the patient and reviewing the subject's medical record. Many of these assessments are routinely done as standard of care at the current time.
Postoperative analgesia will generally consist of scheduled toradol, scheduled Tylenol, MS Contin or Oxycontin, oxycodone PRN, and celebrex 100-200 mg BID or any combination of these. Therapy may be altered for patients with history of drug intolerances or allergies or any other contraindication to a specific therapeutic agent. Extended release opioid therapy may also be excluded in select elderly patients at the discretion of the orthopedic team. This therapy represents standard of care and is not altered by study involvement.

24 and 48-hours post-operative Follow-up:
The patient will be assessed on the floor for pain at rest, pain with activity, opioid consumption, nausea, pain disturbing sleep, location of most severe pain and satisfaction with regional anesthesia technique will be ascertained at 24 and 48 hours following the surgical procedure by questioning patient and review of medical record. Pain with be assessed using a Numerical Rating Scale (NRS) (0-10) where 0 represents no pain and 10 represents the worst pain imaginable. Duration of hospitalization will be obtained from review of medical record. Subjects with new or persistent complaints at 48 hours post-surgery that could be related to the study procedures will be offered continued follow-up by telephone or in-hospital room visit until the complaints resolve. Follow-up procedures would depend greatly on the clinical presentation but could include imaging, specialist consultation or surgical intervention. Subjects without complaints will be given appropriate information for contacting the research team if such complaints arise.

Physical therapy will determine pain with physical therapy, quadriceps strength, passive flexion/extension range of motion, postoperative quadriceps strength, postoperative adductor strength, and 10 meter walk test (gait velocity) at 24 and 48 hours postoperatively. All measurements of strength will be done using the Kiio Sensor. Based on physical therapy team experience, patients are currently able to ambulate 10 meters in approximately 45 seconds on postoperative day one with 20 ml of local anesthetic injected into the adductor canal. The physical therapy team feels that ambulation velocity is generally limited by weakness and pain. However, we do not currently know if decreasing the dose of local anesthetic injected into the adductor canal will result in improved ambulation resulting from increased strength or worsened ambulation performance secondary to increased pain.

Concomitant Medications:
Analgesic and anti-emetic requirements for block placement, intraoperatively, in PACU, at 24 hours, 48 hours and during course of hospitalization will be extracted from the patient's electronic medical record.

### 7.1 Data entry
Information extracted from the subject's medical records includes date of service, subject name, date of birth, medical record number, age, gender, height, weight, data pertaining to the subject's pain, opioid consumption and ASA classification. In addition, SF12 mental component and physical component, WOMAC and Knee Society Score, UCLA activity score, preoperative range of motion and degree of varus/valgus deformity will be collected from the medical record.

All study data will be collected by a study team member on a standardized case report form (CRF) (see Appendix B) and transferred to an electronic Microsoft Excel spreadsheet suitable for export in coded format to a statistical analysis program. Data entry into electronic format will take place on a private computer away from potential viewing by non-study personnel. The paper and electronic data will be kept in the primary investigator's locked office in the Department of Anesthesiology. The computer will be pass-coded and linked to a secure Anesthesia Department server to allow access only to approved study personnel. At the end of seven years, all identifiable data will be destroyed as required by UWHC.

### 7.2 Subject withdrawals

At any point prior to or during the intervention period, the subject's clinical care team or a study physician may decide the subject should be withdrawn from the study. If a subject is withdrawn from the study for any reason the subject will then be followed according to the standard of care follow-up plan.

Study intervention will immediately stop and subject's clinical care team and a study physician will be immediately notified if one of the following occurs:

1) The subject suffers a severe adverse perioperative outcome that precludes participation in physical therapy or measurements of motor strength or sensory examination

In the event the study method is terminated, the reason for termination will be documented on a case report form.

## 8. Data analysis and statistical considerations

All data will be summarized using standard descriptive statistics, including mean, standard deviation, minimum, maximum, median, inter-quartile range, and confidence intervals, as appropriate. The data will be presented graphically (where possible) using scatter plots, profile plots, or histograms. Data analyses will be performed on an intent-to-treat basis using SAS (SAS Institute Inc., Cary, NC; version 8.2 or greater) or Minitab (Quality Plaza, State College, PA; version 13.0 or greater). The primary analyses will consist of comparing the three study volumes of injection for superiority. For all tests, statistical significance will be defined as a p-value less than 0.05. ANOVA and two-sample t-test will be used to compare the data between the three groups or between any two individual groups. Repeated measures ANOVA will be used to analyze multiple follow-up data points. Patients with missing longitudinal data will be handled by either using data imputation methods to replace the missing data or via the use of repeated measures ANOVA to better approximate the average values at each time point**.** Bonferroni correction will be utilized to counteract the problem of multiple comparisons and control the familywise error rate.

### 8.1 Sample size determination

This study is a randomized, three group (5, 10, 20 ml bupivacaine), mixed study using the primary endpoint of ambulation or gait velocity over 10 meters (10 meter walk test) on POD 1. The data from this preliminary study will be used to generate hypotheses for future trials. We performed an effect size calculation based on the ratio of the hypothesized differences and the standard deviation based on our current experience. Based on physical therapy team experience, patients are currently able to ambulate 10 meters in approximately 45 seconds on postoperative day one with 20 ml of local anesthetic injected into the adductor canal. The physical therapy team feels that ambulation velocity is generally limited by weakness and pain. However, previous retrospective research done at our own institution demonstrated that adductor canal block patients were able to ambulate more effectively than those patients receiving a femoral nerve catheter (i.e. those with a more profound motor blockade). We therefore hypothesize that decreasing the dose of local anesthetic delivered into the adductor canal will decrease the amount of time required to ambulate 10 m and that this difference could approach 15 seconds. We hypothesize that the standard deviation may be of similar magnitude. With a power of 0.8 and significance level of 0.05, 16 patients are required per group. Increasing enrollment to 20 patients per group will allow for patient drop out.

## 9. Risks and benefits of trial participation

### 9.1 Potential risks

It is possible that larger volumes of local anesthetic could track proximally within the adductor canal and result in significant motor weakness to the quadriceps muscle. Significant weakness may be a risk factor for falls. It is also possible that decreased volumes may result in increased pain and difficulty participating with physical therapy. Inherent risks associated with nerve blockade include bleeding, infection, nerve damage, allergic reaction to local anesthetic, etc. However, standard of care is currently for patients presenting for TKA to receive an adductor canal block and therefore these would not represent additional risks.

***Risks associated with loss of confidentiality***

There is a risk that information recorded about subjects will be shared with people who would not normally have access to this information.

***Unknown risks***

This study may involve risks to the subject which are currently unforeseeable. We will inform subjects as soon as possible if we discover any information that may affect the subject's health, welfare, or decision to be in this study.

### 9.2 Mitigation of potential risks

The risk of increased quadriceps weakness and fall will be minimized by the involvement of physical therapists for all postoperative motor strength evaluations. The risk of inadequate analgesia will be minimized by the availability of supplemental oral and potentially intravenous analgesics.

### 9.3 Potential benefits and risk-to-benefit ratio

While there are risks to involvement in this research trial, they generally should be infrequent and not difficult to manage. The potential benefits of this research could result in quicker hospital discharge time with resulting decreases in costs. Patients may also benefit from a decreased risk of infection if they are able to leave the hospital sooner or improved implant function if early postoperative rehabilitation is optimized.

## 10. Adverse events and unanticipated problems

### 10.1 Adverse event definitions

***Adverse event (AE)***

An adverse event is defined as any untoward or unfavorable medical occurrence in a human subject including any abnormal sign, symptom, or disease temporally associated with the SSACNB or study procedure that appears or worsens during the study or study follow-up period. AEs may be anticipated (e.g., redness/soreness at injection site) or unanticipated (e.g., bleeding/infection/nerve damage). Adverse event information will be collected throughout the study from informed consent through resolution of the AE and documented on the case report form or the standard follow-up questionnaire.

All AEs (anticipated and unanticipated) will be recorded on one of the study data sheets (case report form or standard questionnaire) by a study investigator or study staff. In the event of an unanticipated AE, the primary anesthesia team caring for the subject will intervene as deemed appropriate. These are the same provisions that would be made for any non-study case and represents standard practice.

***Serious adverse event (SAE)***

A serious adverse event is defined as any adverse event that meets one of the following criteria:

- Results in death; OR
- Is life-threatening; OR
- Requires hospitalization or prolongs existing hospitalization; OR
- Results in significant or persistent disability or incapacity; OR
- Results in a congenital anomaly/birth defect

Given the minimal risk associated with the use of SSACB and the study procedures, no serious adverse events (SAEs) are anticipated. If a SAE occurs, the study primary and co-primary investigators will be immediately notified and further enrollment in the study will be halted until a full explanation of the cause of the event and its relationship to the SSACB and/or study procedure is understood. The IRB will be notified and re-initiation of study enrollment will not occur until approved by the IRB.

***Unanticipated problem (UP)***

An unanticipated problem is defined as an event that meets all of the following criteria:

1) Unexpected in severity, nature, or frequency given the research procedures and the characteristics of the subject population (i.e., problems that are not described in this protocol or other study documents); AND
2) Related or possible related to participation in the research; AND
3) Suggests that research places subjects or others at a greater risk of harm related to the research than was previously known or recognized.

### 10.2 Severity assessment

The severity of all adverse events will be assessed according to the following scale:

- Mild = not requiring treatment or intervention
- Moderate = resolved with treatment/intervention
- Severe = inability to carry on normal activities and required professional medical attention

### 10.3 Causality assessment

The Site PI will determine the relationship of adverse events to the research intervention using the following scale:

- Definite = AE is clearly related to the study procedures
- Probable = AE is likely related to the study procedures
- Possible = AE is possibly related to the study procedures
- Unlikely = AE is doubtfully related to the study procedures
- Unrelated = AE is clearly not related to the study procedures

Additionally, AEs will be considered "probably related" to study procedures if one of the following happens:

- Fall; OR
- Local anesthetic toxicity or allergy

### 10.1. Procedures for recording and reporting adverse events

All serious adverse events that occur from the time the subject provides informed consent through and including 28 calendar days after the procedure will be recorded. Non-serious adverse events that occur from the time the study procedures begin to the end of the last study visit will be recorded.

### 10.4 Other reportable events

Reporting timeframes begin when the site learns of the occurrence of the event.

| Event | Definition | Reporting |
|---|---|---|
| Breach of confidentiality | The exposure of any study information or communications directly related to a study subject to anyone not named as study staff or the release of a study subject's identifiable information to study staff who were not specified to receive such information in the protocol or IRB application. | Treat as major deviation (below) |
| Protocol deviation | A deviation is an incident involving a departure from the IRB-approved protocol in the actual conduct of the study. Deviations may result from the action of the participant, investigator, or staff. | See below |

| Event | Definition | Reporting |
|---|---|---|
| Major deviations | Deviations are considered major when the unapproved change(s) in previously approved research activities, implemented without IRB approval, may potentially adversely affect subjects' rights, safety, welfare, or willingness to continue participation, or affect the scientific design of the study and/or the integrity of the resultant data. | Treat as an Unanticipated Problem (above) |
| Minor deviations | Deviations are considered minor when the unapproved change(s) in previously approved research activities, implemented without IRB approval, do not adversely affect subjects or the integrity of the study data. | Sites are to report cumulative events to AE Coordinator at time of continuing review. |
| Protocol violation | An incident involving an intentional deviation from the IRB-approved protocol that was not implemented in response to an emergency situation and that may impact a subject's rights, safety, and/or welfare, makes a substantial alteration to risks to subjects, or affects the scientific design of the study and/or the integrity of the resultant data. Violations may also be repeated deviations (major or minor) of the same nature. Violations can represent serious or continuing non-compliance with the federal regulations and guidelines for ethical conduct of human subject research. | Treat as an Unanticipated Problem (above) |
| Protocol Exceptions | A protocol exception is an IRB-approved deviation for a single subject or a small group of subjects, but is not a permanent revision to the research protocol. | Protocol exceptions must be approved by local IRB prior to implementation. |

## 11. Trial safety monitoring

### 11.1 Data Safety Monitoring Committee

After 15 subjects have been recruited, the study data will be reviewed by an independent anesthesiologist, blinded to study arm assignment, to ensure that no safety concerns exist. In the unlikely event that there is a safety concern, study recruitment will be halted and an independent Data Safety Monitoring Committee (DSMC), consisting of a minimum of three qualified practitioners, will be convened to evaluate the safety concern and make recommendations regarding changes to the study methods or termination of the study.

## 12. Administrative requirements

### 12.1 Good clinical practice

The study will be conducted in accordance with FDA and ICH guidelines for Good Clinical Practice. All study staff will be thoroughly familiar with the contents of this protocol and associated trial materials.

### 12.2 Data quality assurance

Paper records containing personal identifying information will be stored in the study primary investigator's locked office and destroyed after seven years as required by UWHC.

### 12.3 Study monitoring

After 30 subjects have been recruited, the study data will be reviewed by an independent anesthesiologist, blinded to study arm assignment, to ensure that no safety concerns exist. In the unlikely event that there is a safety concern, study recruitment will be halted and an independent data safety board, consisting of a minimum of three qualified practitioners, will be convened to evaluate the safety concern and make recommendations regarding changes to the study methods or termination of the study.

### 12.4 Ethical consideration

The study will be conducted in accordance with ethical principles founded in the Declaration of Helsinki. The IRB will review all appropriate study documentation in order to safeguard the rights, safety and well-being of the subjects. The study will only be conducted at sites where IRB approval has been obtained. The protocol, informed consent form, written information given to the patients, safety updates, annual progress reports and any revisions to these documents will be provided to the IRB by the investigator.

### 12.5 Patient confidentiality

Subject privacy and confidentiality will be ensured by restricting access to personal identifying study data only to members of the research team. In addition, as mentioned previously, recruitment will take place in the subject's cubicle or room in the preoperative or preprocedural holding area with the curtain drawn or door closed, in a tone of voice insufficient for others to overhear the conversation and in the presence of only those immediately accompanying the subject and those who are directly involved with the subject's care.

### 12.6 Investigator compliance

The investigator will conduct the trial in compliance with the protocol approved by the IRB. Changes to the protocol will require written IRB approval prior to implementation, except when the modification is needed to eliminate an immediate hazard(s) to subjects.

### 12.7 Subject cost and payment

***Cost***

Subjects will not incur additional costs due to their participation in this study.

***Payment***

Subjects will not be paid for participation in this study.

## 13. Funding sources

Funding will be provided by the Department of Anesthesiology's Research and Development (R&D) Committee.

## 14. Publication Policy

## References

1. Kardash K, Hickey D, Tessler MJ, Payne S, Zukor D, Velley AM. Obturator versus femoral nerve block for analgesia after total knee arthroplasty. Anesth Analg 2007;105:853-858.
2. Macalou D, Trueck S, Meuret P, Heck M, Vial F, Ouologuem S, Capdevila X, Virion JM, Bouaziz H. Postoperative analgesia after total knee replacement: the effect of an obturator nerve block added to the femoral 3-in-1 nerve block. Anesth Analg 2004;99:251-254.
3. McNamee DA, Parks L, Milligan KR. Post-operative analgesia following total knee replacement: an evaluation of the addition of an obturator nerve block to combined femoral and sciatic nerve block. Acta Anaesthesiol Scand 2002;46:95-99.
4. Bergeron SG, Kardash KJ, Huk OL, Zukor DJ, Antoniou J. Functional outcome of femoral versus obturator nerve block after total knee arthroplasty. Clin Orthop Relat Res 2009;467:1458-1462.
5. Sato K, Sai S, Shirai N, Adachi T. Ultrasound guided obturator versus sciatic nerve block in addition to continuous femoral nerve block for analgesia after total knee arthroplasty. Japanese Clinical Medicine 2011;2:29-34.
6. Kapoor R, Adhikary SD, Siefring C, McQuillan PM. The saphenous nerve and its relationship to the nerve to the vastus medialis in and around the adductor canal: an anatomical study. Acta Anaesthesiol Scand 2012;56:365-367.
7. Saranteas T, Anagnostis G, Paraskeuopoulos T, Koulalis D, Kokkalis Z, Nakou M, Anagnostopoulou S, Kostopanagiotou G. Anatomy and clinical implications of the ultrasound-guided subsartorial saphenous nerve block. Reg Anesth Pain Med 2011;36:399-402.
8. Mudumbai SC, Kim E, Howard SK, Workman JJ, Giori N, Woolson, Ganaway T, King R, Mariano ER. Continuous adductor canal blocks are superior to continuous femoral nerve blocks in promoting early ambulation after TKA. Clin Orthop Relat Res 2013 Epub.
9. Kwofie MK, Shastri UD, Gadsden JC, Sinha SK, Abrams JH, Xu D, Salviz EA. The effects of ultrasound-guided adductor canal block versus femoral nerve block on quadriceps strength and fall risk. A blinded, randomized trial of volunteers. Reg Anesth Pain Med 2013;38:321-325.
10. Henningsen MH, Jaeger P, Hilsted KL, Dahl JB. Prevalence of saphenous nerve injury after adductor-canal-blockade in patients receiving total knee arthroplasty. Acta Anaesthesiol Scand 2013;57:112-117.

11. Andersen HL, Gyrn J, Moller L, Christensen B, Zaric D. Continuous saphenous nerve block as a supplement to single-dose local infiltration analgesia for postoperative pain management after total knee arthroplasty. Reg Anesth Pain Med 2013;2:106-111.
12. Jaeger P, Zaric D, Fomsgaard JS, Hilsted KL, Bjerregaard J, Gyrn J, Mathiesen O, Larsen TK, Dahl JB. Adductor canal block versus femoral nerve block for analgesia after total knee arthroplasty. A randomized, double-blind study. Reg Anesth Pain Med 2013;38:526-532.
13. Jenstrup MT, Jaeger P, Lund J, Fomsgaard JS, Bache S, Mathiesen O, Larsen TK, Dahl JB. Effects of adductor-canal-blockade on pain and ambulation after total knee arthroplasty: a randomized study. Acta Anaesthesiol Scand 2012;56:357-364.
14. Kim DH, Goytizolo EA, Kahn RL, Maalouf DB, Manohar A, Pattt ML, Goon AK, Lee YY, Ma Y, YaDeau JT. Adductor canal block versus femoral nerve block for total knee arthroplasty. A prospective, randomized, controlled trial. Anesthesiology 2014;120:540-550.
15. Casati A, Bariarello M, Di Cianni S, Danelli G, De Marco G, Leone S, Rossi M, Fanelli. Effects of ultrasound guidance on the minimum effective anaesthetic volume required to block the femoral nerve. British J of Anaesh 2007;98:823-827.
16. Maffiuletti NA. Assessment of the hip and knee muscle function in orthopaedic practice and research. J Bone Joint Surg Am 2010;92:220-229.

**Appendix D – Kiio Information Sheet**

Kiio Inc. began the Phase I "WiFi-enabled hand-portable real-time force sensor to objectively assess strength" project on March 1, 2013, and concluded the project August 1, 2013. (Expenditures prior to March 1, 2013 were borne by Kiio.) This is the final summary report for the Phase I project. **Kiio successfully completed all Phase I Aims.** No changes were made to the project's goals and aims as outlined in the original Phase I Research Strategy.

The **overall project goal of Phase I** was to refine, miniaturize, and test a clinically relevant prototype device (the kiio™) that would be able to accurately and consistently measure force over time so as to provide kinetic measurement of muscle strength, continuously tracking variability in strength over the entire range of movement to enable a complex analysis of muscle performance. Our goals for the kiio were that it should (1) provide wireless data output via proprietary software to PCs in real-time, allowing a clinician to track and interpret data as the patient generates it; (2) offer high inter-rater reliability for consistency between clinicians; (3) interface with commonly used rehabilitative equipment such as resistance cables; (4) be hand-portable, not requiring dedicated clinic space; (5) be cost effective in terms of initial investment and clinician training; and (6) be rugged enough to withstand the rigors of daily use while maintaining accuracy. Its clinical significance would be to provide a fast, objectively valid, reliable, portable and cost-effective method of strength assessment, thus eliminating a significant barrier to the implementation of evidence-based evaluation and outcome measurement in prescriptive rehabilitative exercise.

**Aim 1: Develop and prototype a functional, integrated kiio to measure continuous muscle force output and translate this information to a real-time digital data stream.** Kiio began with a high-level, logical engineering model of the device in block diagrams depicting a device able to generate force readings using off-the-shelf components and proprietary software. We developed an electrical and logical design for a printed circuit board (PCB) using Computer assisted engineering software (CAE). We created protocols to test the PCB design and identify and remove errors, while keeping functional design elements. Successive iterations eliminated design errors and added functionality, leading to a stable design. We wrote firmware (hard-coded proprietary programming) to control the microprocessor, and synchronized the WiFi transceiver and a wireless router to ensure the proper communication between the kiio and a PC, necessary to display data in real-time.


**Figure 1**

**Figure 2**

**Table 2: Phase I, Aim 1 outcomes**

| Task | Objective outcomes/Milestones | Result |
|---|---|---|
| 1.1 | Hand-portability: kiio prototype will be no larger than 7 x 4 x 10 cm and no heavier than 150 g. | **Success.** kiio weighs just 120g and measures 7cm wide x 9cm high x 4cm deep (see **Figure 1**) |
| 1.2 | Design elements: kiio prototype will include: a) a strain gauge, b) a microprocessor, c) a wireless WiFi transmitter, and d) an Li-ion battery | **Success.** kiio includes a strain gauge, microprocessor, wireless WiFi transmitter and a rechargeable Li-ion battery |
| 1.3 | Integration with commonly-used rehabilitative exercise equipment: kiio prototype will connect to a variety of commonly used resistance mechanisms | **Success.** kiio connects directly to commonly-used resistance mechanisms such as elastic cables, straps, and portable handles (see **Figure 2**) |
| 1.4 | WiFi data delivery: kiio prototype will send a continuous, real-time digital WiFi data stream to a PC | **Success.** kiio sends a continuous, real-time digital data stream wirelessly over WiFi of force readings over time to a computer as described and tested in Aims 2 & 3 |

**Table 3 - Device Results**

| Load Cell | Kiio #7E | Delta |
|---|---|---|
| 0.1 | 0.3 | 0.2 |
| 5.1 | 5.2 | 0.1 |
| 10.3 | 10.3 | 0.0 |
| 15.2 | 15.0 | -0.2 |
| 20.7 | 20.4 | -0.3 |
| 25.8 | 25.7 | -0.1 |
| 30.8 | 30.9 | 0.1 |
| 35.8 | 36.4 | 0.6 |
| 40.9 | 41.4 | 0.5 |
| 46.0 | 46.3 | 0.3 |
| 51.3 | 51.6 | 0.3 |
| 56.0 | 56.6 | 0.6 |
| 61.0 | 61.5 | 0.5 |
| 66.2 | 66.4 | 0.2 |
| 71.3 | 71.4 | 0.1 |
| 76.4 | 76.6 | 0.2 |
| 81.3 | 81.6 | 0.3 |
| 86.5 | 86.6 | 0.1 |
| 92.1 | 92.1 | 0.0 |
| 97.4 | 97.1 | -0.3 |
| 103.1 | 102.8 | -0.3 |

**Aim 2: The kiio prototype will be iteratively calibrated to ensure that it properly reads known force and can be set to ignore a tare weight.** The kiio requires calibration for precision and consistency; without it, accuracy and test-retest reliability would be jeopardized. Kiio used a six step process (**Figure 3**) to facilitate this Aim. Ensuing successful completion of the setup steps, we tested 10 devices by repeatedly hanging the 20 plates (one at a time) on each device. With each additional plate the weight was allowed to settle and kiio reported a static force reading to the PC where it was recorded. Cumulative readings of these weights were also taken using a commercially available load cell for comparison.

**Figure 3 - Steps to prepare kiio for static testing**

| Step | Action |
|---|---|
| 1 | Establish two sets of known weights |
| a | Kettlebells for creating callibration curves |
| b | ~5 lb. plates for static device testing |
| 2 | Create calibration software for kiio |
| 3 | Establish callibration equation for each device |
| 4 | Calibrate kiio by loading equation into device memory |
| 5 | Create Tare (Zero-out) software for kiio |
| 6 | Tare kiio by loading offset into device memory |

**Summary of Test Results:** All ten devices were initially calibrated and had tare weights set. Nine out of ten devices were accurate to within 2% (1.0 lb) on the first pass (i.e., without the need for a re-calibration or re-tare). Their average deviation from the load cell ranged from 0.11 lbs. to 0.83 lbs. with no readings deviating from expected results by more than 1.0 lb. Only one device (#7E) exceeded our target tolerance, with an average under-weight of 1.18 lbs. per reading. The readings from device #7E were consistently low. Consequently, the device was re-calibrated, re-tared, and the tests were rerun and kiio #7E yielded an average deviation of 0.14 lbs. from the expected results (see **Table 3**). The initial readings of device #7E suggests that our technician did not properly do a full tare (step #6 above) prior to conducting tests.

**Table 4 – Phase I, Aim 2 outcomes**

| Task | Objective outcomes/Milestones | Result |
|---|---|---|
| 2.1 | kiio will correctly measure force and transmit accurate data within the larger of either 2% absolute error or 1 lb. | **Success.** Kiio extended the number of test kiio devices from 4 to 10. All devices successfully completed calibration on their first attempt, and 100% of the force readings were within acceptable tolerance. |
| 2.2 | Redefine of zero point: kiio prototype will be able to accept a constant offset and thereby redefine the zero point, or a given tare weight. | **Success.** A connector was hung from the device and an offset was sent from the PC to the kiio to tare the weight back to 0.0 lbs. 100% of devices were successful. This process was repeated with various connectors, ranging in weight from 0.2 lbs. to 5.1 lbs. Again, 100% of devices were successful in the tare process. |
| 2.3 | Maximum static weight: kiio device will be able to accurately register static weights from 0.0 to 100.0 lbs. | **Success.** The commercial load cell registered a total of 103.1 lbs (99.7% accurate, with possible variability derived from cumulative rounding error over 20 plates). 9 of the 10 kiio devices were accurate to within tolerance on the 1st attempt (i.e., without a need for re-calibration). 100% of kiios met specification after recalibrating and re-taring one device (#7E). |

**Aim 3: Verify the prototype measurements are valid and reliable over high use and extended sessions.** The kiio device must be used rigorously over a high number of repetitions to ensure it maintains accuracy and reliability in order to provide valid and consistent measurements through expected durations of use. The aim contained two stages: (1) Compare the kiio to a calibrated strain gauge for consecutive cycles to analyze statistical variances; and (2) examine accuracy after 20 days of use.

Kiio created a motorized test fixture (**Figure 4**) to exercise 6 devices with a series of cyclical tests. Testing software was used to collect force readings from kiio devices and a commercial load cell. Data was plotted in real-time to the screen, as well as logged to a Microsoft Access database for further analysis in Microsoft Excel.

**Figure 4**

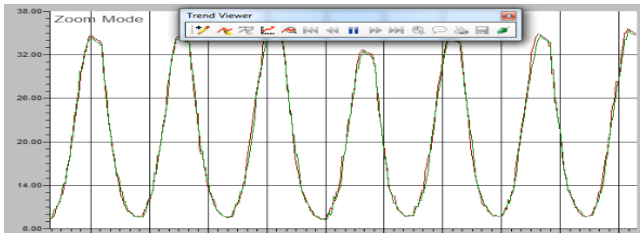


**Figure 5**

Test #1 was to run each device through a series of ~500 cycles of applying a force up to a threshold and then relaxing that force back to a lower limit. Peak values from the kiio for each cycle was analyzed against the peak values from the load cell. 100% of the kiios were within this Aim's accuracy threshold for 100% of these cycles.

Additional analysis of the full 33,000+ samples per device (beyond the scope of the original Aim), demonstrated that the device not only reports peak forces accurately during dynamic use, but tracks well throughout the entire force curve. **Figure 5** is a close-up of data from a kiio device (shown in green) plotted against the load cell (in red). The graph shows that as forces range from 8-36 lbs., the kiio tracks the commercial load cell with amazing accuracy. **Figure 6** shows, for each device, the # of cycles tested and the linear regression analysis $R^2$ and ICC statistics. A typical scatter plot and residual plot is also shown.

| Device ID | Cycles | $R^2$ | ICC(3,1) | 95% CI |
|---|---|---|---|---|
| 60 | 504 | 0.98 | 0.989 | 0.987-0.990 |
| 67 | 500 | 0.99 | 0.995 | 0.995-0.996 |
| 69 | 500 | 0.99 | 0.994 | 0.993-0.995 |
| 6D | 500 | 0.99 | 0.995 | 0.994-0.996 |
| 75 | 493 | 0.99 | 0.993 | 0.992-0.994 |
| 7E | 501 | 0.99 | 0.996 | 0.996-0.997 |

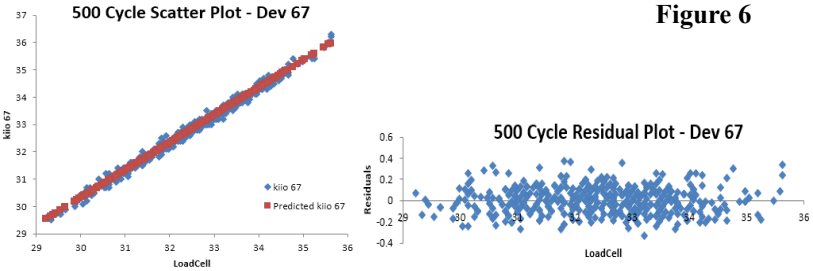


**Figure 6**

Kiio also conducted multiple tests to determine if readings drift over time. In addition to the specified 20 days of dynamic load testing for durations ranging from 10 minutes to 1 hour, we also performed static weights tests 3 months after the device's original calibration. Our conclusion: there's no discernible drift after 3 months of use. **Figure 7** is a summary of statistics for the 20-day testing on 4 kiio devices:

| Device ID | Day 1 | | | Day 20 | | |
|---|---|---|---|---|---|---|
| | $R^2$ | ICC(3,1) | 95% CI | $R^2$ | ICC(3,1) | 95% CI |
| 60 | 0.97 | 0.982 | 0.973-0.988 | 0.98 | 0.99 | 0.985-0.993 |
| 67 | 0.97 | 0.985 | 0.977-0.990 | 0.98 | 0.988 | 0.982-0.992 |
| 69 | 0.98 | 0.992 | 0.988-0.995 | 0.99 | 0.995 | 0.993-0.997 |
| 7E | 0.99 | 0.995 | 0.993-0.997 | 0.99 | 0.989 | 0.983-0.992 |

**Figure**

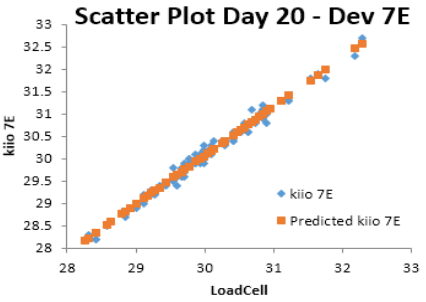


**Table 5 – Phase I, Aim 3 outcomes**

| Task | Objective outcomes/Milestones | Result |
|---|---|---|
| 3.1 | Measurement validity: kiio prototype will accurately measure forces over time as compared to industry calibrated strain gauge (with no more than 2% absolute error, and $R^2 \geq 0.98$) over the course of 500 cycles. | **Success.** 6 out of 6 devices passed this test with 100% of samples taken within this specified tolerance (2998 peak readings from the kiio devices were within 1.0 lb. of the load cell value). The $R^2$ and ICC numbers also verify the accuracy of the kiio device. |
| 3.2 | Reliability: kiio prototype will demonstrate high intra-class correlation coefficients (ICC≥0.99) comparing baseline to tests that recur over time, throughout extended testing periods (10 min. - 1 hr. continuous use) | **Success.** The results of dynamic testing produced the same consistency that static testing exhibited: All readings were within the tolerance of this Aim; kiio is ready to be ruggedized and enter the next phase of testing. |

Kiio has shown prototype kiio devices provide accurate measurements for thousands of use cycles over the course of weeks of continuous use, and that the kiio is capable of use with similar frequency to manual muscle testing in a typical physical therapy clinic by one therapist over the course of a month with no loss of accuracy.

**Successful Completion:** By successfully completing all of the Aims set forth in Phase I, Kiio has demonstrated the feasibility of a hand-portable wireless kiio device prototype. kiio provides objectively valid, reliable measurements of force over time, and accurately transmits this data wirelessly to a PC. This is a major step in Kiio's overall vision of developing the integrated kiio FLEX System: combining the kiio device and kiio FLEX software for Physical and Occupational Therapists (PT/OT's). In Phase II Kiio proposes to further refine and ruggedize the kiio for clinical use, to develop kiio FLEX, create an integrated animated exercise library, and to test the system in clinical settings. Concurrently, we will be completing 510k premarket notification on the kiio FLEX System. The fully developed kiio FLEX System will be positioned to provide PT/OT's a fast, objectively valid, reliable, portable and cost-effective method of strength assessment. This will enable PT/OT's to integrate evidence-based assessments into their practices which could significantly reduce the disability burden on the U.S. population (both individual and societal costs) by enhancing clinical efficiency and increasing positive patient outcomes.