An Open-Label, Parallel, Randomized Study to Evaluate the Performance of Needle Placements for Diagnostic and Therapeutic Neuraxial Procedures, Using a Handheld Tactile Imaging-based Method Versus Palpation

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An Open-Label, Parallel, Randomized Study to Evaluate the Performance of Needle Placements for Diagnostic and Therapeutic Neuraxial Procedures, Using a Handheld Tactile Imaging-based Method Versus Palpation

Version 2 / 25 November 2020

Regulatory Sponsor: IntuiTap Medical, Inc.
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Protocol Identifiers: INT-001

Study Type: Multi-center, Randomized, Superiority Study

Study Product: VerTouch™

Statement of Compliance

This document is a protocol for a human research study. This study will be conducted according to US and International standards of Good Clinical Practice, applicable government regulations and Institutional research policies and procedures.

All individuals responsible for the design and conduct of this study have completed Human Subjects Protection Training and are qualified to be conducting this research prior to the enrollment of any subjects.

As Principal Investigator, I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol. Modifications to the study are acceptable only with an approved protocol amendment. I agree to obtain approval from the IRB and/or regulatory bodies of competent jurisdiction, for the protocol and informed consent before initiating the study, to obtain consent from subjects prior to their enrollment in the study, to collect and record data as required by this protocol and case report forms, to prepare adverse event and study reports as required by this protocol and to maintain study documentation for the period of time required.

_____ _____

[Print Name/Title of Principal Investigator] Date

As a Sub-Investigator, I agree to conduct this clinical study in accordance with the design and specific provisions of this protocol. Modifications to the study are acceptable only with an approved protocol amendment. I agree to obtain approval from the IRB and/or regulatory bodies of competent jurisdiction, for the protocol and informed consent before initiating the study, to obtain consent from subjects prior to their enrollment in the study, to collect and record data as required by this protocol and case report forms, to prepare adverse event and study reports as required by this protocol and to maintain study documentation for the period of time required.

_____ _____

[Print Name/Title of Sub- Investigator] Date
[Print Location if multi-site protocol]

_____ _____

[Print Name/Title of Sub- Investigator] Date
[Print Location if multi-site protocol]
[Add additional sheets as necessary]

Version History

Version #	Approval Date	Significant Changes from Previous Version
Version1	26 Aug 2020	Original Protocol Version
Version 2	25 Nov 2020	Incorporate changes based on FDA pre-submission feedback

Table of Contents

Study Synopsis

Title	An Open-Label, Parallel, Randomized Study to Evaluate the Performance of Needle Placements for Diagnostic and Therapeutic Neuraxial Procedures, Using a Handheld Tactile Imaging-based Method Versus Palpation
Short Title	Study to Evaluate the Performance of Needle Placements for Diagnostic and Therapeutic Neuraxial Procedures
Protocol Numbers	INT-001
Study Sponsor	IntuiTap Medical, Inc.
Study Classification	FDA has determined that the study may proceed under the NSR provisions of the IDE regulation
Study Design	An open-label, parallel, randomized study design
Study Duration	Study duration is anticipated to be approximately 4 months
Study Center(s)	Approximately 3 sites in the United States
Objectives	The primary objective of this study is to establish the superiority of VerTouch versus the conventional palpation technique for the number of insertion attempts required in diagnostic and therapeutic neuraxial procedures.
Number of Subjects	It is expected that approximately 120 subjects will be screened to meet a target enrollment goal of 96 subjects.
Main Inclusion / Exclusion Criteria	**Inclusion Criteria** 1. Males and females aged 18 years and above, inclusive 2. Subjects scheduled for one of the following procedures: • Diagnostic LP (collection of CSF and/or measurement of ICP to diagnose hemorrhaging or neurological infections) • Therapeutic LP (intrathecal injection of therapeutic agents; drainage of CSF to treat pseudotumor cerebri) • Planned orthopedic or obstetric procedure, such as labor/induction, cesarean section,

hysterectomy, or total hip/knee replacement, with neuraxial anesthesia (injection of anesthetic into spinal and/or epidural space to reduce pain during procedure)

- Epidural blood patch (use of autologous blood to close holes in the dura mater and relieve PDPH)

3. Subjects having a BMI $\leq 42 kg/m^2$

Exclusion Criteria

1. Patient does not provide informed consent
2. Skin or soft tissue infection near the puncture site
3. Allergy to local anesthetic
4. Uncorrected coagulopathy
5. Acute spinal cord trauma
6. History of lumbar spinal surgery
7. Prior known failed neuraxial anesthesia
8. Diagnosed scoliosis, thoracic kyphosis, lumbar lordosis, scleroderma, or ankylosing spondylitis, or lumbar spinal stenosis
9. Incarcerated subjects

Study Device	VerTouch™
Duration of Device Exposure	< 2 hours
Reference Therapy	Conventional palpation technique used for spinal needle placement
Endpoints	**Primary Endpoint:**

The number of insertion attempts (any forward movement of the needle following puncture of the skin) in the study device group as compared to the control group (palpation). Attempts are counted until confirmation of spinal canal access can be assessed.

Secondary Endpoints:

1. Incidence of first-insertion success (a case that does not require any reinsertions, but can include any number of redirections)
2. Number of redirections (any forward movement of the

needle in a new direction not preceded by withdrawal from the skin, counted until confirmation of spinal canal access can be assessed)

3. Number of passes (any forward movement of the needle, calculated as the sum of insertions and redirections)
4. Incidence of first-pass success (a case that does not require reinsertions or redirections)
5. Subject discomfort during landmarking on a 100mm VAS scale
6. Provider confidence with the identified insertion site on a 1-5 Likert scale
7. Procedure success as confirmed by the following procedure-specific methods:
    - Epidural anesthesia: able to achieve a T10 or greater bilateral sensory level change to cold
    - Spinal anesthesia: able to achieve sensory blockade to surgical stimulus at level desired
    - Diagnostic and therapeutic LP: return of CSF
    - Blood patch: able to inject homologous blood into epidural space (entry confirmed by loss-of-resistance)

Tertiary Endpoints:

1. Localization time (time from first touch of draped patient to identification of an insertion site; for VerTouch, this is the time from device placement to movement of the applicator to the identified insertion site)
2. Insertion time (time from retrieval of marker or local anesthetic assembly until no further needle advancements are made)
3. Number of bone contacts
4. Incidence of referral to radiology

Safety Endpoints

1. Incidence of post-dural puncture headache (PDPH)
2. Incidence of unintended dural puncture (specific to epidural anesthesia)
3. Incidence of paresthesia during needle insertion (specific to neuraxial anesthesia)
4. Incidence of traumatic tap (results in visible blood

aspiration)

Exploratory Endpoints:

1. Procedure time (from positioning of the patient to removal of the drape from the subject's back)
2. Incidence of conversion from spinal to epidural (specific to neuraxial anesthesia)

Statistical Methods

The primary endpoint will be analyzed using a bootstrap approach for the null hypothesis that VerTouch requires more insertions than palpation. A one-sided 0.025 p-value will be considered as the cut-off for statistical significance.

Abbreviations

2D	2-Dimensional
AE	Adverse Event
BMI	Body Mass Index
CI	Confidence Interval
CFR	Code of Federal Regulations
CRNA	Certified Registered Nurse Anesthetist
CV	*Curriculum Vitae*
eCRF	Case Report Form
EM	Emergency Medicine
ESI	Epidural Steroid Injection
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICH	International Conference on Harmonization
IFU	Instructions for Use
IRB	Institutional Review Board
ITT	Intent to Treat
LA	Local Anesthetic
LP	Lumbar Puncture
NP	Nurse Practitioner
NSR	Non-Significant Risk
OTC	Over the Counter
PA	Physician's Assistant
PDPH	Post-Dural Puncture Headache
PM	Pain Medicine
PHI	Protected Health Information
PP	Per Protocol
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
UADE	Unanticipated Adverse Device Effect
US	United States
VAS	Visual Analog Scale

1 Study Contact Information

1.1 Sponsor Contact Information

IntuiTap Medical, Inc.
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1.2 Key Study Personnel

1.2.1 Clinical Coordinator

ICON Clinical Research LLC
2100 Pennbrook Parkway
North Wales, PA 19454

1.2.2 Clinical Study Monitor

ICON Clinical Research LLC
2100 Pennbrook Parkway
North Wales, PA 19454

1.2.3 Medical Monitor

ICON Clinical Research
888-723-9952 (Telephone)

1.2.4 Statistician

Stat One, LLC
2880 Slater Road, Suite 105
Morrisville, NC 27560

2 Introduction / Background and Rationale

2.1 Background

Neuraxial procedures, in which a needle is inserted into the spinal canal through a gap in the vertebrae, are performed at a rate of nearly 13 million per year in the US, across a myriad of diagnostic and therapeutic clinical scenarios. Among these are the 800,000 lumbar punctures (LPs) conducted to diagnose subarachnoid

hemorrhage or neurological infection, or to treat neurological diseases[1]. There are also 3.1 million deliveries of neuraxial anesthesia to reduce pain during obstetric and orthopedic procedures, such as labor/induction, hysterectomy, and total hip/knee replacement[2,3]. Additionally, there are 9 million epidural steroid injections (ESIs) for back and leg pain relief[4]. Finally, there are epidural blood patch procedures, in which autologous blood is used to close holes in the dura mater and relieve post-dural puncture headache (PDPH).

The standard of care involves manual palpation of the patient's back to detect the spinous processes (SPs) and estimate the location of the interspinous needle insertion site[5,6]. While providers are trained to perform these procedures with meticulous precision and attention to detail, this technique remains highly inaccurate, often requiring multiple insertion attempts to properly place the needle[7,8]. These attempts lead to patient pain and complications, such as traumatic taps and PDPHs; unpredictable procedure times; and poor facility throughput[9,10]. The challenge is only exacerbated in patients with high body mass index (BMI), a factor that already accounts for 13.8% of procedure failures, and is only worsening in the US[11,12].

Challenging cases are often referred to radiology for fluoroscopic guidance, at rates greater than 47% in settings such as emergency medicine (EM)[13]. However, fluoroscopy exposes patients and providers to unnecessary radiation, can rarely be used in perioperative settings, and is associated with high costs for overhead, patient transport, and assembly of a radiology team[14-16]. Ultrasound may also be used to help visualize the vertebrae in challenging cases[17]. However, the modality requires significant training on how to interpret its output, and is cumbersome, requiring a gel medium and manipulation of a needle in combination with an unstable probe.

VerTouch™ is a novel device that holds promise to reduce the ambiguity associated with the palpation technique, and to overcome the shortcomings of other imaging-based solutions. VerTouch employs scanning-based tactile imaging to detect spinal landmarks, analogous to those sensed during palpation[18]. When pressed against the subject's lower back, the Device's imaging component detects the differences in hardness surrounding the spinous processes. In real-time, data collected by the device are processed and visualized as the TactoMap™, a 2D pressure map on a full-color display, from which the operator can accurately and intuitively identify a suitable insertion site. VerTouch can be used to mark the identified site with a supplied surgical marker, or to inject local anesthetic and place an introducer or spinal needle to a safe depth at that site. The Device is then removed, and the procedure is completed in the standard manner.

VerTouch has the potential to require minimal training, cause no additional discomfort to the patient, and be seamlessly integrated into any neuraxial procedure. By providing the information needed to reveal the underlying lumbar anatomy, VerTouch has the potential to help the provider identify an accurate insertion site, and have a greater likelihood of success on the first insertion attempt. With the potential to reduce the number of needed insertions, VerTouch may reduce the frustration, pain, and complications associated with these procedures, and standardize the time associated with both the localization and insertion steps. Combined, these potential benefits may translate into lower associated costs of care for factors like bed and boarding time, as well as readmissions and/or further treatment[19-21].

2.2 Rationale

This study is intended to evaluate the use of VerTouch to reduce the number of insertion attempts compared to the conventional manual palpation technique.

3 Device Description

VerTouch is a handheld device, which is capable of assembly and use by a single operator, and requires no connection with peripheral systems or software during clinical use[22,23]. VerTouch includes reusable and disposable parts (**Figure 1**).

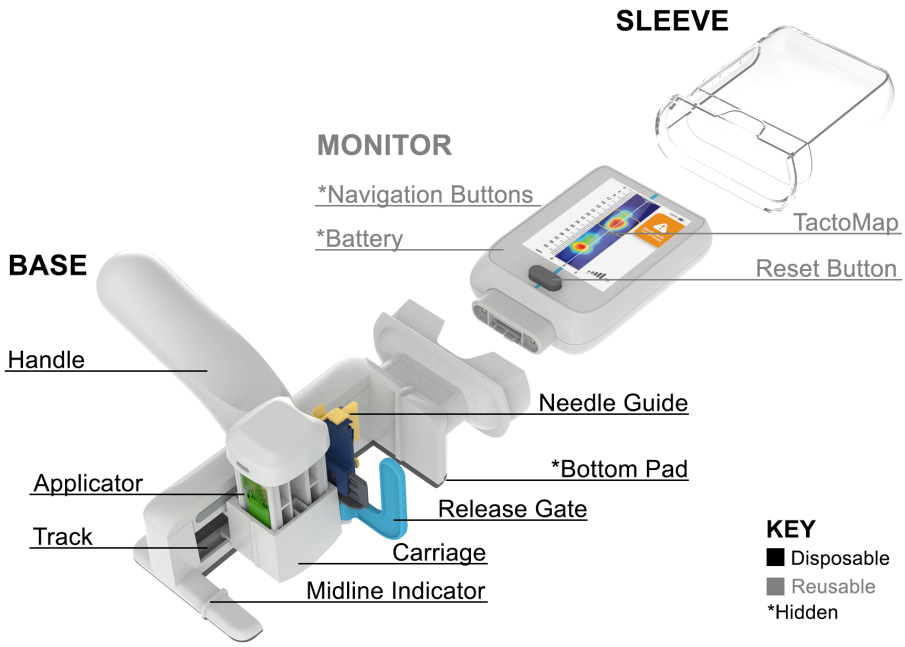


Figure 1. *Exploded, oblique view of VerTouch subsystems, including the disposable Base and Sleeve, and reusable Monitor. In this figure, 'needle guide' broadly references all needle and marker guidance elements, including the Restrictor.*

Not shown are the reusable Charging Station, Power Adapter, and PC Connector, none of which are directly used for clinical operation; as well as the Disposable Packaging, which includes a dedicated mini surgical Marker, and a Dock to facilitate sterile assembly of VerTouch components.

The reusable Monitor is the subsystem that performs image acquisition, processing, and display of the TactoMap. It comprises a rechargeable battery, and is sold with a charging station to support repeated use. The disposables include a device Base and a Sleeve, both of which are single use, and provided terminally sterilized via ethylene oxide (EtO). The Base allows for placement of the device against the back, and includes the interactive components for scanning-based imaging and needle or marker guidance; while the Sleeve prevents contamination from the Monitor during use. Further description on these components can be found below; please see the Instructions for Use (IFU)[24] for more detail and illustrations.

3.1 Assembly

The sterile disposable components, including the Base, the Sleeve, and a dedicated surgical Marker are supplied in a two-part tray. The Tray is wrapped in a Drape, which is used to create a sterile field for the device. The wrapped Tray comes in a sealed Pouch, along with a disposable Dock, which is used to permit sterile electromechanical assembly between the disposable Base and reusable Monitor. The Device powers on upon assembly, after which the sleeve can be slid over the Monitor, forming the protective barrier.

3.2 Workflow Selection

VerTouch can be used to support needle insertion via any of three workflows: marking, placement of a 20-22G, 3.5” or 5” needle, or placement of an introducer. With the marking workflow, the device is used to mark an identified insertion site, but local anesthetic (LA) injection and needle insertion occur after device removal. With the introducer and needle placement workflows, LA is injected, and the needle or introducer is placed to a safe depth, through a depth-limiting mechanism (Restrictor) integrated into the device (**Figure 2**; see Section 9.2.1 for further description).

The remainder of the insertion is then completed after Device removal, which is enabled by a Needle Release Gate (Gate). Prior to beginning the procedure, the user selects their target workflow. If pursuing a marking workflow, the Needle Guide can be removed by pulling up the Removal Tab, which reveals the larger-diameter Marker Guide, and replaced later, if needed.

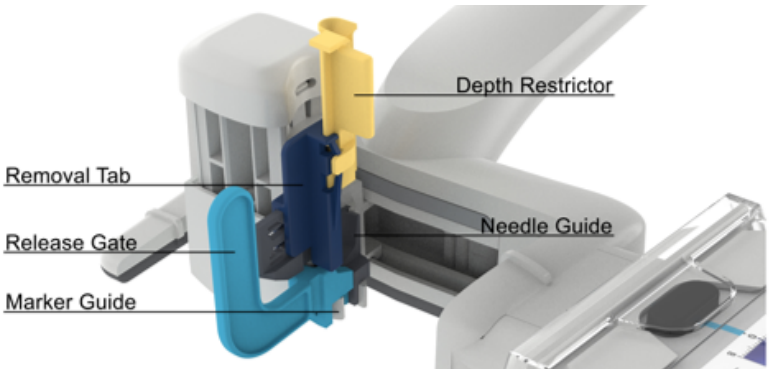


Figure 2. *Oblique view of Needle Guide, with Restrictor in 5"-needle position.*

3.3 Device Placement

With VerTouch, users continue to use standard landmarking techniques to identify a safe level for the procedure area. This is typically done by palpating for the tips of the iliac crest, which approximately align with the L4-5 interspinous space. This is performed prior to draping the patient, such that the procedure area is exposed and used to guide Device placement. After Device assembly, the user then grips the Handle on the Base with his/her left hand, and places the assembled Device against the patient's back. Midline indicators on the Device can be used to support alignment with the midline of the spine. A rubber Bottom Pad on the Base prevents slippage of the Device along the back during use.

3.4 Imaging

The Applicator is the primary component that facilitates scanning-based tactile imaging. A calibrated, piezoresistive sensor array (Sensor) is mounted to the patient-contacting surface of the Applicator, which is designed to optimize feature resolution with minimal application of force (**Figure 3**).

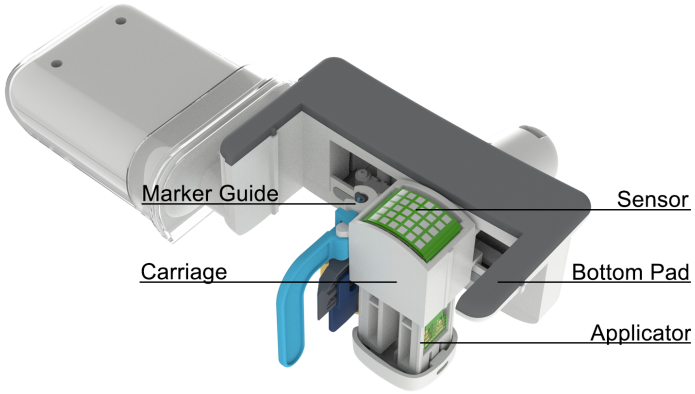


Figure 3. *Bottom view of assembled VerTouch, highlighting sensor mounting.*

The Applicator is assembled with a Carriage mechanism that is mounted to a fixed Track the length of at least two SPs in the indicated patients. Via an Applicator Button accessible by the user's right hand, the Applicator can be slid along the craniocaudal (y) axis via the Track; and can be pressed along the anteroposterior axis (z), via a spring mechanism that facilitates 2 cm of tissue penetration. A flexible printed circuit board assembly (PCBA) connects the Sensor to downstream electronics and allows for free y- and z-axis movement; an elastomeric (y-lock) strip ensures that the Applicator cannot slide while being pressed. When the user presses the Applicator at a first location, a linear positioning system is used to display the corresponding 2D pressure data at that location within the imaging range on the screen. The user then slides the Applicator to a new location, and repeats the process until the imaging range is complete. A Force Gauge on the screen (not included in **Figure 3**) indicates the approximate force of each press to help the user apply the same force across presses. Throughout the imaging process, the user observes the outputted pressure data with the goal of identifying a blue region along the midline corresponding to an interspinous space. Navigation Buttons on the left side of the Monitor (not visible in **Figure 3**) can be used to adjust screen brightness and/or scanning sensitivity during imaging. In the event of any misalignment and/or the lack of an interspinous space, the image can be reset via an operator-facing Reset Button on the Monitor, and scanning can be performed at a new location.

3.5 Insertion

The Needle Guide is reversibly attached to the top (cranial side) of the Applicator, and its location is presented as a crosshair overlay in the imaging screen. Once an insertion site is identified, the user slides the Applicator until the crosshair aligns with that site. If a marking workflow has been selected, the user places the Marker directly through the exposed Marker Guide. He/she then removes the Device, and injects LA and inserts his/her preferred needle on the mark. For the placement workflows, LA is first injected directly through the Needle Guide. For introducer placement, the user then places the introducer through the Needle Guide. The Gate is then opened, which allows the Device to be removed from the partially placed introducer. Following Device removal, the introducer is fully inserted and the preferred spinal needle is placed through it. The same is done for needle placement; however, to ensure the needle does not exceed a safe depth while the device is in place, the earlier-described Restrictor is used. The Restrictor is pushed over to align with the Needle Guide for placement of a 3.5" needle; and it is further pulled up for placement of a 5" needle (***Figure 4***). Locking mechanisms ensure the Restrictor locks in both positions.

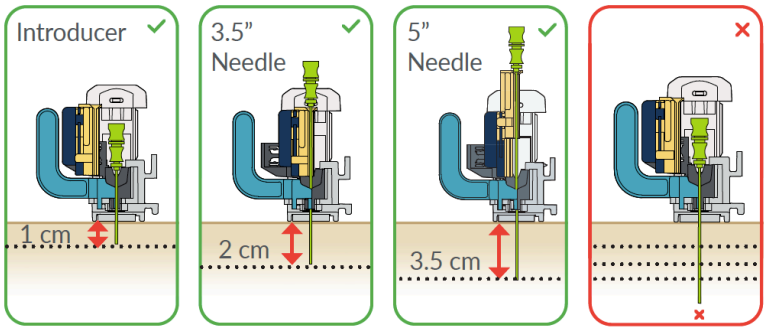


Figure 4. *Side view (cranial) of VerTouch Needle Guide, depicting Restrictor configurations for safe placement of an introducer, and 3.5" and 5" needle, extracted from the IFU*[24].

After needle placement, the Gate is opened to allow the device to be pulled away from the introducer or needle. This accomplished by sliding the Device downward, craniocaudally; and then leftward, mediolaterally (as viewed against the patient's back).

With any workflow, the ability of the system to assist with accurate insertion-site identification has the potential to be associated with a reduction in insertion attempts, although some redirections may still be necessary considering the fixed, perpendicular orientation of the Needle Guide. All Needle and Marker Guide interactions are performed with the right hand, per standard needle insertion training, regardless of handedness.

3.6 Disassembly

Upon needle access to the spinal canal, the user completes his/her procedure per standard protocol. Following the procedure, the Sleeve and Monitor are disconnected from the Base. The Monitor is dropped into the dock, while the remaining components are disposed of with other disposable procedure components.

3.7 Monitor Maintenance

After each use, the Monitor is cleaned for visible contaminants. It is then brought to a storage location and placed on the VerTouch Charging Station. The Power Adapter is used to connect the Charging Station to an outlet for Monitor recharging. Note that the Device cannot be used while charging, as the Base and Charging Station connect to the same connection port on the Monitor.

For study use, the Charging Station also has a data transfer port that allows for connection to a PC for transfer of study data that can be referenced when

investigating anomalous findings and/or can be used to establish a database of human TactoMaps for future development. For a given subject, firmware in the Monitor captures pressure data corresponding to the final scan that was used to identify an insertion site. Sampled at a rate of at least 10Hz, these include Sensor readings before and after integration into the full scanning range (referred to as push images and built images, respectively). Also included is header information for each sample, including the current timestamp, sensitivity value, linear position value, and force level. To provide additional information, users can flag the frame at which the Applicator was moved to align the Needle Guide with their identified site by pressing and holding the central Navigation Button on the Monitor. Data transfer software is loaded onto on-site study PCs, which allows for upload of these data from the Monitor following each procedure.

3.8 Maintenance Mode

VerTouch also has a touchscreen-enabled maintenance mode, which can be operated by a non-clinical user to adjust time and date settings, and/or to perform password-protected firmware updates.

3.9 User and Subject Characteristics

Patients undergoing neuraxial procedures have varying characteristics, though most receiving neuraxial anesthesia for obstetric procedures are pregnant. Indicated patients have a BMI of $\leq 42 kg/m^2$ and may be in the seated or lateral decubitus position.

The Device is intended for use by all providers credentialed to perform these procedures. **Table 1** summarizes some such providers, as well as procedure-specific information, such as the VerTouch workflow(s) applicable to each procedure.

Table 1. *Intended Users and Procedures*

Name	Applicable Workflow(s)	Settings	Locations	Providers
Diagnostic LP	Needle placement, marking	EM	Emergency Room	EM Physician, PA
		NE	Neurology Suite	Neurologist, Neurosurgeon, PA
Therapeutic LP	Needle placement, marking	NE	Neurology Suite	Neurologist, Neurosurgeon, PA
Neuraxial Anesthesia	Marking, introducer placement	AN	Operating Room	Anesthesiologist, CRNA
Blood Patch	Marking	AN	Operating Room	Anesthesiologist, CRNA
ESI	Marking	PM	PM Suite	PM Physician, PA, CRNA
		AN	Operating Room	Anesthesiologist, PA, CRNA
PA = physician assistant; CRNA = certified registered nurse anesthetist; NE = neurology, AN = anesthesiology (includes obstetric and orthopedic); PM = pain medicine				

Note that users may have either handedness, and be seated or standing during use. MDs may include residents (a type of clinical trainee), fellows, and attendings. Not listed below are nurse practitioners (NPs), who are credentialed to perform neuraxial procedures in some facilities. In some states, anesthesiology assistants (AAs) may also perform these procedures in the anesthesiology setting.

3.10 Intended Use

VerTouch has not yet been cleared by FDA, and is intended to aid in the localization of an interspinous space, and the placement of a needle at the identified site, for diagnostic and therapeutic spinal punctures, including LPs, neuraxial anesthesia (spinals, epidurals, and combined spinal-epidurals), ESIs, and epidural blood patches. The device includes functionality to guide a marking tool or needle.

All investigational devices will have the following label statement: **CAUTION – Investigational Device. Limited by Federal (or United States) Law to Investigational Use.**

4 Device Accountability

4.1 Device Receipt

IntuiTap Medical will ship devices directly to the clinical sites, to the attention of the Investigator or designee at that site. Device receipt and inventory procedures will be determined by the individual sites' standard operating procedures. At a minimum, a device inventory log will record device serial numbers for reusables and disposables, date of receipt, and disposition. At least two sets of reusable VerTouch components will be provided to each clinical setting within each site.

4.2 Device Storage

Devices will be stored in secured rooms under ambient conditions, which meet VerTouch storage requirements. Reusable monitors will be stored on VerTouch charging stations as described earlier; disposables will be stored in their sterile packaging. Device access will be controlled by the Site Investigator or designee.

4.3 Device Dispensing

For each procedure, disposable units will be dispensed for use by the Site Investigator as per the allocation scheme; paired with one of the reusable monitors available within the clinical setting. Device serial numbers will be recorded on the subject's case report form. Device records will be reconciled at each monitoring

visit. This reconciliation will be logged on the device accountability form, and signed and dated by the designated study team member.

4.4 Device Disposition

At the conclusion of the study, all reusable study components, including monitors, charging stations, power adapters, and PC connectors are to be returned to the Sponsor. Consumable components will be recorded and disposed of in accordance with local medical waste regulations. Device return will be recorded and reconciled with device assignment and accountability records.

4.5 Return or Destruction of Unused Devices

Following a full product reconciliation, all unused devices are to be returned to IntuiTap Medical at the address listed below.

IntuiTap Medical, Inc.
965 W Chicago Ave.
Chicago, IL 60642

5 Study Objectives

The primary objective of this study is to establish the superiority of VerTouch versus the conventional palpation technique for the number of needle insertion attempts required in diagnostic and therapeutic neuraxial procedures.

6 Study Design

6.1 Overview of Study Design

After Informed Consent is obtained, subjects will be randomized 1:1 into two groups via the block randomization method with a list held in each test setting. Standard landmarking techniques will be used in both groups to identify the procedure area. For subjects randomized to the tactile-imaging group (T), VerTouch will be used to identify an interspinous space and to place a marker, introducer, or needle. For subjects randomized to the palpation group (P), the palpation-landmarking method will be used. After marker, introducer, or needle placement, the procedure will continue in the usual manner for subjects in both groups (**Figure 6**).

A designated study observer within each setting will record the time to identify an insertion site; time to place the marker, introducer, or needle; number of insertions, re-directions, and bone contacts (counted until confirmation of spinal canal access

can be assessed); incidence of procedure success; subject's level of discomfort during landmarking; and provider's level of confidence with the identified insertion site. Total procedure time, incidence of traumatic taps, and incidence of referrals to radiology or pain management will be recorded in all settings. In anesthesiology, incidences of paresthesia, unintended dural puncture, and conversion from spinal to epidural anesthesia, will be collected for exploratory analysis, where applicable. Any usability issues or device malfunctions observed during the clinical study will also be documented.

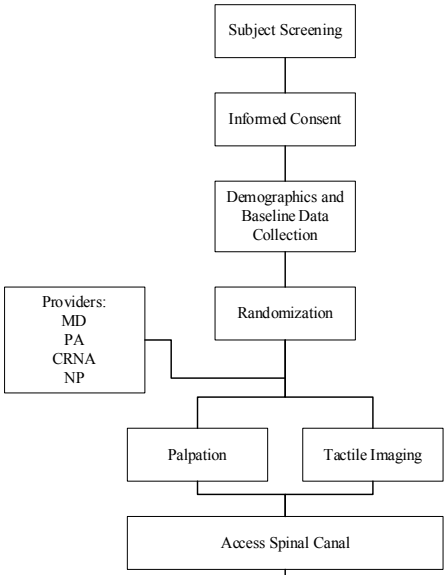


Figure 5. *Overall Study Design*

Although spinal punctures in all clinical settings involve the same localization and insertion processes, there may be variations in setting, subject, and/or provider characteristics. While early VerTouch testing has not evidenced any corresponding variations in device usability and/or outcomes associated with these variations, the study is designed to capture them.

Accordingly, EM, neurology, and anesthesiology settings will be approximately evenly represented in the study, with at least 24 subjects enrolled in each. To adequately represent patients undergoing obstetric and orthopedic procedures, enrolled anesthesiology subjects will be approximately evenly split between these sub-settings. The PM setting will not be included in the study, as there are limitations, particularly with respect to reimbursement, for ESIs performed with palpation or other non-fluoroscopic techniques. However, PM providers will be represented in IntuiTap's summative usability study, and undergo the same

anesthesiology training as those clinical study investigators specialized in obstetrics and orthopedics.

Additionally, investigators will form a representative sample of typical neuraxial procedure providers, including MDs (residents, fellows, and attendings), PAs, and CRNAs, where applicable. Residents must be in their second post-graduate year and above, having performed at least 5 neuraxial procedures in the past 12 months, and are considered trainees. Apart from their level of training, investigators should have a representative range of relevant experience, indicated by the approximate number of neuraxial procedures they have performed in the past year. To ensure adequate user variability, a single investigator should perform no more than 20% of procedures in his/her setting (corresponding to a minimum of approximately 6 procedures per investigator). Any provider type not included in the study will have been assessed in formative and/or summative human factors testing.

6.2 Anticipated Duration of the Clinical Investigation

Study duration is anticipated to be approximately 4 months.

6.3 Evaluation Criteria / Effectiveness and Safety

6.3.1 Primary Clinical Endpoint

The number of insertion attempts (any forward movement of the needle following puncture of the skin) in the study device group as compared to the control group (palpation). Attempts are counted until confirmation of spinal canal access can be assessed.

6.3.2 Secondary Clinical Endpoint(s)

1. Incidence of first-insertion success (a case that does not require any reinsertions, but can include any number of redirections)
2. Number of redirections (any forward movement of the needle in a new direction not preceded by withdrawal from the skin, counted until confirmation of spinal canal access can be assessed)
3. Number of passes (any forward movement of the needle, calculated as the sum of insertions and redirections)
4. Incidence of first-pass success (a case that does not require reinsertions or redirections)
5. Subject discomfort during landmarking on a 100mm VAS (See Section 17.1)

6. Provider confidence with the identified insertion site on a 1-5 Likert scale (See Section 17.2)
7. Procedure success as confirmed by the following procedure-specific methods:
    - Epidural anesthesia: able to achieve a T10 or greater bilateral sensory level change to cold
    - Spinal anesthesia: able to achieve sensory blockade to surgical stimulus at level desired
    - Diagnostic and therapeutic LP: return of CSF
    - Blood patch: able to inject homologous blood into epidural space (entry confirmed by loss-of-resistance)

6.3.3 Tertiary Endpoints

1. Localization time (time from first touch of draped patient to identification of an insertion site; for VerTouch, this is the time from device placement to movement of the applicator to the identified insertion site)
2. Insertion time (time from retrieval of marker or LA assembly until no further needle advancements are made)
3. Number of bone contacts (counted until confirmation of spinal canal access can be assessed)
4. Incidence of referral to radiology

6.3.4 Safety Endpoints

1. Incidence of post-dural puncture headache (PDPH)
2. Incidence of unintended dural puncture (specific to epidural anesthesia)
3. Incidence of paresthesia during needle insertion (specific to neuraxial anesthesia)
4. Incidence of traumatic tap (results in visible blood aspiration)

6.3.5 Exploratory Endpoints

1. Procedure time (from positioning of the patient to removal of the drape from the subject's back)
2. Incidence of conversion from spinal to epidural (specific to neuraxial anesthesia)

6.4 Study Population

Subjects admitted to EM, neurology, or anesthesiology settings that require a neuraxial procedure as part of their management or work up, and that meet inclusion and exclusion criteria will be approached by research staff for enrollment in the study. Spinal punctures in these clinical settings involve the same localization and insertion processes, through access to the spinal canal. Written informed consent will be obtained in person by the study coordinator or designee.

6.4.1 Sample Size

It is expected that approximately 120 subjects will be screened to meet a target enrollment goal of 96 subjects (48 in each group) across 3 investigational sites.

The superiority hypothesis for the number of insertion attempts with IntuiTap (μ_1) and palpation (μ_2) is:

$$H_0: \mu_1 \geq \mu_2 \text{ vs } H_1: \mu_1 < \mu_2$$

The sample size was selected based on historical information and previous clinical trial data collected with the VerTouch device. A literature survey identified eight (8) papers where the mean and standard deviation (SD) for insertions for palpation were identified[25-32]. The definitions appear similar to the proposed endpoint. The mean attempts ranged from 1.3 to 3.3 and SD ranged from 0.0 to 6.9. A weighted average of the means and standard deviations provided an average of mean of 2.3 and SD of 2.8[33]. Based on the spread of individual results, a mean of 2.1 and SD of 1.5 was considered a reference for the power analysis.

A sample of 81 attempts was available for the VerTouch device across several iterations of the device. Of the attempts, 90% were successes on the first attempt and the mean number of attempts was 1.1 and SD was 0.6.

In order to assess the sample size, given the truncated nature of the distribution and the planned use of a bootstrap analysis, a simulation study was performed. Random vectors were built by taking the ceiling of absolute values of a mixture for two normal distributions to build long-tailed distributions with means and standard deviations similar to those above. Analyses were done using a bootstrap analysis of the difference in means, Wilcoxon Test, T-test with unequal means, and a T-test of log-transformed data. For a sample size of 24 subjects per group, the bootstrap analysis,

Wilcoxon Test, and T-test of log-transformed data had at least 92% power while a T-test of the observed counts had 89% power.

In addition, an estimate of the secondary endpoint of first attempt success of approximately 50% was obtained in the simulation exercise for palpation. The planned sample size of 48 per group provides 90% power when compared to a first attempt success rate of 81% in the VerTouch group. Hence, the study is also expected to have adequate power for the primary analysis and the secondary endpoint of success on the first insertion.

6.4.2 Subject Recruitment

Subjects will be recruited from investigators practicing at large hospital settings from Anesthesiology, Neurology or the Emergency Departments. Those departments will be used to recruit subjects into this study.

6.4.3 Subject Screening

Following Informed Consent, subjects will be screened for eligibility. Height and weight will be recorded, and BMI calculated. Scheduled date of eligible procedure will be recorded. Relevant medical history and age will be assessed for concordance with inclusion and exclusion criteria. Subjects who do not meet eligibility criteria will be recorded as Screen Failures. At subject screening, subjects will be given a subject ID number that encodes both investigational site and subject number.

6.4.4 Prior and Concomitant Medications

There are no restrictions on prior or concomitant medications. However, concomitant prescription and over the counter (OTC) pain and anti-anxiety medications must be recorded in the source documentation and in the eCRF.

6.4.5 Inclusion Criteria

Subjects will be eligible to participate in the study if **all** of the following conditions exist:

1. Males and females aged 18 years and above, inclusive
2. Subjects scheduled for one of the following procedures:
    - Diagnostic LP (collection of CSF and/or measurement of ICP to diagnose hemorrhage or neurological infection)
    - Therapeutic LP (intrathecal injection of therapeutic agents; drainage of CSF to treat pseudotumor cerebri)

- Planned orthopedic or obstetric procedure, such as labor/induction, cesarean section, hysterectomy, or total hip/knee replacement, with neuraxial anesthesia (injection of anesthetic into spinal and/or epidural space to reduce pain during procedure)
- Epidural blood patch (use of autologous blood to close holes in the dura mater and relieve PDPH)

3. Subjects having a BMI $\leq 42 kg/m^2$

6.4.6 Exclusion Criteria

Subjects will be excluded from participation in the study if **any** of the following conditions exist:

1. Patient does not provide informed consent
2. Skin or soft tissue infection near the puncture site
3. Allergy to local anesthetic
4. Uncorrected coagulopathy
5. Acute spinal cord trauma
6. History of lumbar spinal surgery
7. Prior known failed neuraxial anesthesia
8. Diagnosed scoliosis, thoracic kyphosis, lumbar lordosis, scleroderma, ankylosing spondylitis, or lumbar spinal stenosis
9. Incarcerated subjects

6.4.7 Exit / Discontinuation Criteria

Subjects will exit the study if any of the following conditions exist:

1. Subject voluntarily withdraws from the study.
2. Subject death.
3. Subject acquires any of the listed exclusion criteria.
4. Subject completes the protocol.
5. Subject's well-being, in the opinion of the Investigator, would be compromised by study continuation.

7 Study Procedures

7.1 Informed Consent

All prospective subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. The consent form will be submitted

with the protocol for review and approval by the IRB for the study. The formal consent of a subject, using the IRB-approved consent form, must be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent. A blank copy of the IRB-approved form must be kept on-site and by the Investigator.

Subjects who sign an informed consent will be considered enrolled in this study. Subjects who provide consent for participation but do not meet all study eligibility criteria will be considered screen failures.

7.2 Vulnerable Populations

As noted above adolescent subjects (18-21 years) will be eligible for participation in this study. Pregnant women will be recruited for the cohort including obstetric procedures, such as labor/induction and cesarean section, and eligible to participate in other cohorts as well.

Other recognized vulnerable populations will not be targeted for recruitment, however individual subjects within vulnerable populations may be enrolled. The Human Subject's Protections procedures employed in this protocol are sufficient to protect the rights and welfare of any subject within an eligible vulnerable population and no additional measures are necessary.

7.3 Randomization Scheme

Qualifying subjects will be randomized 1:1 via a block randomization scheme to either the tactile-imaging group (T) or the palpation group (P) within each setting (e.g. EM, neurology, or anesthesiology).

7.4 Clinical Procedures

7.4.1 Visit 1

Screening

At the screening visit the following activities and information will be collected:

- Informed Consent
- Physical Examination (height/weight)
- Eligibility Determination
- Randomization and Subject ID Assignment

- Demographics (gender, age, race, ethnicity)
- Relevant Medical History
- Concomitant Medications

At Treatment

At the time of treatment, the following activities and information will be collected:

- Concomitant Medications
- Pain and/or anti-anxiety medication(s) given for the procedure
- Provider level of training (e.g. resident, fellow, attending, PA, CRNA, NP)
- Provider number of years of in practice
- Provider experience (i.e. number of neuraxial procedures performed in the past 12 months)
- Provider specialty (i.e. emergency medicine, neurology, anesthesiology)
- Procedure setting (i.e. emergency medicine, neurology, orthopedic anesthesiology, obstetric anesthesiology)
- Type of neuraxial procedure (i.e. diagnostic LP, therapeutic LP, spinal anesthesia, epidural anesthesia, CSE, blood patch)
- Reason for Neuraxial Procedure (if not diagnostic LP or blood patch), such as:
    - Therapeutic LP: CSF drainage, intrathecal injection, other
    - Orthopedic procedure: total hip replacement, total knee replacement, other
    - Obstetric procedure: labor/induction, cesarean section, hysterectomy, tubal ligation, other

The subject will be treated with the device or control, per **Figure 6** below (see IFU for more detailed VerTouch steps)[24]. Initial landmarking for vertebral level is performed by standard technique in both groups in order to identify a safe level when placing the drape to expose the procedure area.

Listed data will be recorded in source documentation, by a member of the study team designated as an observer, as they become available. The observer will also be responsible for counting needle insertions and redirections. Note that procedure success may be reported at different points within the treatment, depending on when spinal access can be confirmed for the particular neuraxial procedure.

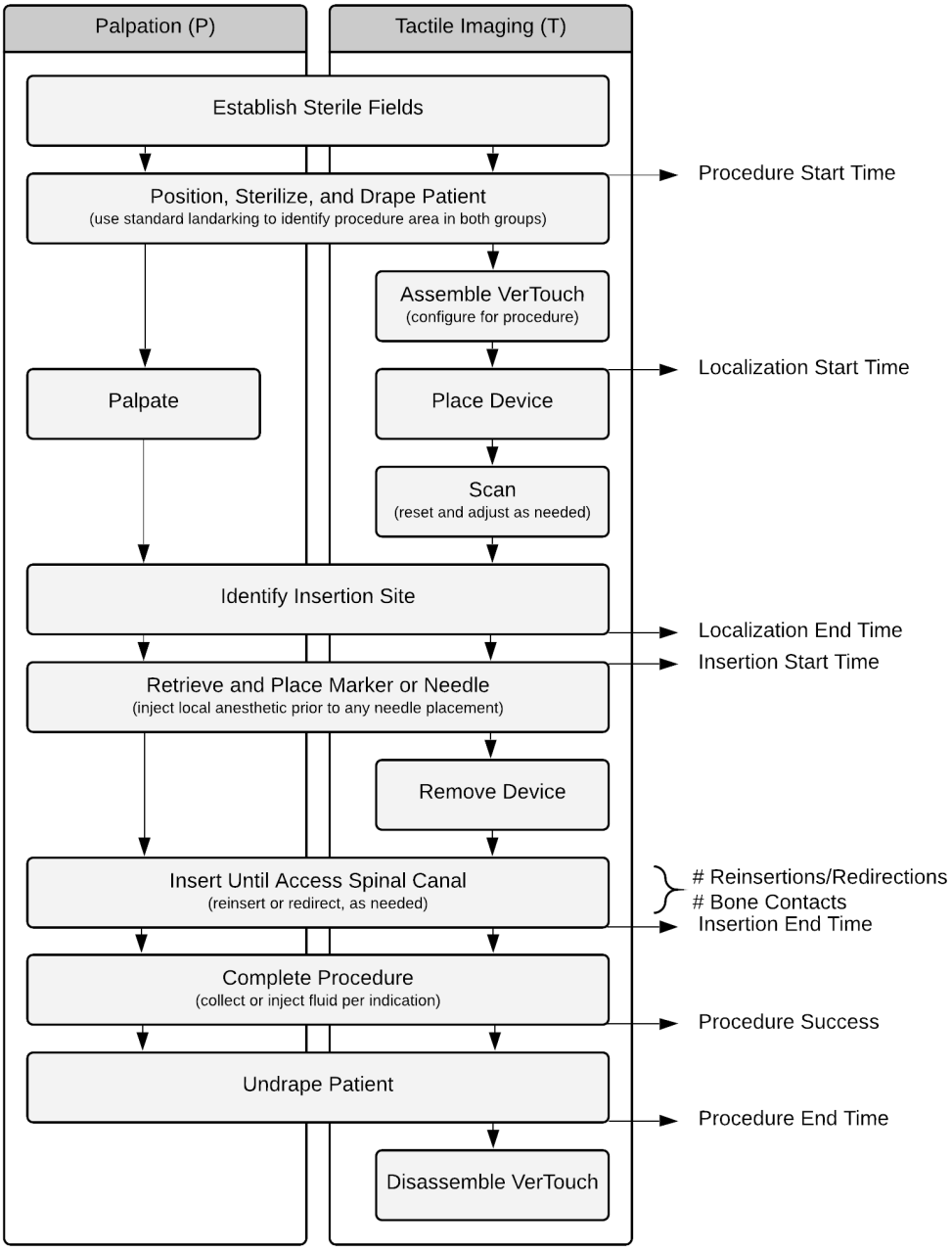


Figure 6. *Flowchart of Visit 1 treatment.*

Post-Treatment

After the completion of the procedure, the following activities and information will be collected:

- Patient position (seated, lateral decubitus)

- Length, gauge, bevel (cutting, non-cutting), and type (straight, curved) of needle used
- VerTouch workflow followed (N/A (control group), marking, introducer placement, needle placement)
- Calculation of number of re-insertions (1 less than insertions)
- Incidence of first-insertion success (1 insertion, any number of redirections)
- Calculation of number of passes (sum of insertions and redirections)
- Incidence of first-pass success (1 pass)
- Calculation of localization, insertion, and procedure times (based on start and end times)
- Incidence of traumatic tap
- Incidence of referral to radiology
- Incidence of conversion from spinal to epidural (neuraxial anesthesia only)
- Incidence of paresthesia (neuraxial anesthesia only)
- Incidence of PDPH
- Intensity of PDPH (mild, moderate, severe)
- Incidence of unintended dural puncture (epidural anesthesia only)
- Subject Discomfort Assessment
- Provider Confidence Assessment
- Adverse Event Assessment
- Upload of data from VerTouch

Post-procedure, the subject will be monitored for adverse events, adverse device effects or other reportable observations to ensure safety, entering relevant data into the eCRF. At the conclusion of the visit, the subject will be released and considered complete. After each procedure, imaging data from VerTouch will be uploaded by the designated observer to a study portal to support investigation of any anomalous finds and/or establishment of a human image database.

7.4.2 Visit 2

Visit 2 must occur at 3 ± 2 days following Visit 1. Phone, or other appropriate follow-ups will be made at Visit 2 to assess the presence and intensity of PDPH in subjects, and assess potential adverse events. At the conclusion of Visit 2, a Subject Study Exit CRF will be completed.

7.5 Follow-Up Procedures and Therapy Transitions

Adverse events identified in the study will be followed to resolution. No additional follow-up procedures or therapy transitions are required.

7.6 Study Timetable / Schedule of Events

Table 2. *Schedule of Events*

	Visit 1			Visit 2
Assessment	Screening	Treatment	Post-Treatment	Follow-up
Demographics	X			
Medical History	X			
Physical Exam (Height & Weight)	X			
Inclusion/Exclusion Criteria	X			
Informed Consent	X			
Randomization	X			
Concomitant Medications	X	X		
Procedure Completion		X		
Discomfort Assessment			X	
Provider Satisfaction Assessment			X	
PDPH			X	
Adverse Event Assessment		X		X
Adverse Device Effect Assessment		X		X

7.7 Deviations from the Clinical Protocol

The study will be conducted as described in this protocol. Investigators are not permitted to deviate from this protocol except to protect patient rights, safety, or well-being. Any deviations from this protocol must be documented by the Investigator. A description of the deviation from the protocol and justification must be recorded on the Protocol Deviation Form. If an emergency situation arises in which the rights, safety or well-being of a subject may require immediate alternative intervention, the Investigator should act in the best interest of the subject. Sponsor and the site's IRB must be notified immediately if this occurs. This should be followed with written confirmation that describes the emergency action and outcomes, to Sponsor and per IRB reporting requirements.

Protocol deviations will be reviewed during routine monitoring visits. Investigators will be required to identify preventive and corrective actions to prevent further deviations. An Investigator may be disqualified from the study for repeated and/or egregious protocol deviations.

7.8 Subject Withdrawal

Subject withdrawals are not anticipated due to the short nature of the subject participation in the study. If a subject withdraws, a Study Exit CRF will be completed.

7.9 Subject Compensation

Subjects will receive no payment or stipend for participation in this study.

8 Data Collection and Analysis

8.1 Subject Population(s) for Analysis

The study populations are defined as follows:

- Intent-to-treat population (ITT): Consists of all randomized subjects according to their randomized group.
- Per-protocol population (PP): Consists of all subjects who received their randomized treatment, did not have an inclusion or exclusion violation, had a procedure success, and did not have a major protocol deviation.

The primary analysis and all study results will be analyzed using the ITT population. The primary analysis will be repeated using the PP population.

8.2 Statistical Methods

This section describes the planned statistical analyses for this study. A detailed Statistical Analysis Plan (SAP) will be completed and placed on file prior to enrollment. The SAP will contain a comprehensive explanation of the methodology used in the statistical analyses described below.

All CRF data will be made available in data listings or in Excel spreadsheets. Data listings will be sorted by subject and visit date, or adverse event onset date. All statistical analyses will be based on the available data. The study results will be reported in summary tables using standard descriptive statistics. Standard numeric descriptive statistics include the n (number of non-missing observations), mean, median, minimum value, and maximum value. Categorical data will be summarized using the counts and percentages based on the non-missing values.

Statistical analyses will be performed to assess the homogeneity of the study populations, evaluate the primary hypothesis, and evaluate the impact of covariates on the performance of the VerTouch device. Standard statistical tests used for

hypothesis testing are the t-test for numeric measures and the likelihood ratio chi-square test for categorical variables. For categorical variables with small cell counts (less than 5), Fisher's exact test will be used. For inferential analyses, unless otherwise indicated, a two-sided p-value of less than or equal to 0.05 will be considered statistically significant. All confidence intervals (CIs) will be two-sided 95% intervals. Note that p-values reported for tertiary and exploratory endpoints will be used for reporting but would not be used in product labeling.

8.2.1 Adjustments for Multiplicity

The study has a single primary endpoint needed for the superiority analysis. If that analysis reaches statistical significance, then the following additional hypothesis of the secondary variables will be considered sequentially such that if one analysis is statistically significant, then the next hypothesis can be evaluated to control for the Type I error for these analyses:

Additional Hypothesis 1: The null hypothesis that the binary rate of first-attempt success is the same in both groups will be analyzed using a likelihood ratio test (H_0: $p_1 = p_2$ vs H_1: $p_1 \neq p_2$ where p_1 is the success rate in VerTouch subjects and p_2 is the success rate in control subjects). The results will be considered statistically significant if the two-sided p-value is less than 0.05 and the VerTouch success rate is higher than the control rate).

Additional Hypothesis 2: The null hypothesis that the mean number of redirections is the higher in the VerTouch subjects compared to the control group using a T-test with unequal variance assumption (H_0: $\mu_1 \geq \mu_2$ vs H_1: $\mu_1 < \mu_2$ where μ_1 is the mean in VerTouch subjects and μ_2 is the mean in control subjects). The results will be considered statistically significant if the one-sided p-value is less than 0.025.

Additional Hypothesis 3: The null hypothesis that the mean number of passes is the higher in the VerTouch subjects compared to the control group using a T-test with unequal variance assumption (H_0: $\mu_1 \geq \mu_2$ vs H_1: $\mu_1 < \mu_2$ where μ_1 is the mean in VerTouch subjects and μ_2 is the mean in control subjects). The results will be considered statistically significant if the one-sided p-value is less than 0.025.

Additional Hypothesis 4: The null hypothesis that the binary rate of first-pass success is the same in both groups will be analyzed using a likelihood ratio test (H_0: $p_1 = p_2$ vs H_1: $p_1 \neq p_2$ where p_1 is the success rate in VerTouch subjects and p_2 is the success rate in control subjects). The results will be

considered statistically significant if the two-sided p-value is less than 0.05 and the VerTouch success rate is higher than the control rate).

Additional Hypothesis 5: The null hypothesis that the mean subject discomfort rated during landmarking from 0 to 10 is higher in the VerTouch subjects compared to the control group using a T-test with unequal variance assumption (H_0: $\mu_1 \geq \mu_2$ vs H_1: $\mu_1 < \mu_2$ where μ_1 is the mean in VerTouch subjects and μ_2 is the mean in control subjects). The results will be considered statistically significant if the one-sided p-value is less than 0.025.

Additional Hypothesis 6: The null hypothesis that the mean provider confidence with the identified insertion site rated 1 to 5 is lower in the VerTouch subjects compared to the control group using a T-test with unequal variance assumption (H_0: $\mu_1 \leq \mu_2$ vs H_1: $\mu_1 > \mu_2$ where μ_1 is the mean in VerTouch subjects and μ_2 is the mean in control subjects). The results will be considered statistically significant if the one-sided p-value is less than 0.025.

Additional Hypothesis 7: The null hypothesis that the binary rate of procedure success is the same in both groups will be analyzed using a likelihood ratio test (H_0: $p_1 = p_2$ vs H_1: $p_1 \neq p_2$ where p_1 is the success rate in VerTouch subjects and p_2 is the success rate in control subjects). The results will be considered statistically significant if the two-sided p-value is less than 0.05 and the VerTouch success rate is higher than the control rate).

8.2.2 Primary Effectiveness Analysis

The study is designed to evaluate whether the use of the VerTouch device is able to reduce the number of insertion attempts to successfully access the spinal canal in a spinal puncture as compared to the conventional palpation technique. The primary hypothesis test will be performed by a bootstrap analysis resampling the cases in each group. The null hypothesis for the analysis is:

$$H_0: \mu_1 \geq \mu_2 \text{ vs } H_1: \mu_1 < \mu_2$$

Where μ_1 is the mean attempts in the VerTouch group and μ_2 is the mean for palpation.

This hypothesis will be evaluated using a bootstrap analysis with a one-sided 0.025 test to indicate statistical significance. The results will be presented for the difference in means and the associated 95% CI; and the ratio of the VerTouch mean divided by the palpation mean and the associated 95% CI.

The primary analysis will include the total insertions for each subject regardless of success on the final placement attempt.

The following supporting analyses will be performed:

- The primary analysis will be performed only for subjects who had a procedure success.
- If there are missing data, best- and worst-case imputation analyses will be performed. For the worst-case imputation, the highest observed value will be imputed in the VerTouch group and the lowest value in the palpation group. The best-case analysis reverses the pattern of imputations.
- A Wilcoxon rank-sum test will be used to evaluate the null hypothesis that median attempts are the same in both arms using a two-sided test with a p-value less than or equal to 0.05 considered significant.
- Homogeneity of the log-transformed count results will be assessed using an ANOVA with site, treatment, and site-treatment interaction terms. A p-value for the site-treatment interaction of less than or equal to 0.15 will be considered statistically significant for this analysis. The n, mean, and SD of values by study site will be provided by treatment group.
- The observed attempts will be evaluated through a t-test for unequal variances comparing the difference in the log (insertion attempts) for each group. The difference will be transformed with the exponent function to provide the ratio of the geometric mean attempts and a two-sided 95% CI for the ratio.

The following subgroups will be considered in exploratory covariate analyses:

- BMI (kg/m^2): underweight (<18.5), normal (18.5-24.9), overweight (25-29.9), class 1 obesity (30.0-34.9), class 2-3 obesity (≥35 .0)
- Age (years): adolescent (<22), young adult (22-40), middle-aged adult (41-65), older adult (>65)
- Provider type: MD, PA, CRNA, AA, NP
- Provider specialty: emergency medicine, neurology, anesthesiology
- MD level (MDs only): resident, fellow, attending
- Provider years in practice: <5, 5-10, >10
- Provider experience (number of neuraxial procedures in past 12 months): 5-25, 26-50, 51-100, >100

- Neuraxial procedure: diagnostic LP, therapeutic LP, neuraxial anesthesia, blood patch
- Medication given for procedure: none, pain, anti-anxiety
- Needle type: spinal 20-22G cutting, spinal 20-22G non-cutting, spinal >22G, Tuohy, CSE
- VerTouch workflow (VerTouch subjects only): marking, introducer placement, needle placement

Subgroup levels will only be considered if there are at least 8 subjects within the covariate level across both treatments.

8.2.3 Additional Analyses

The tertiary and exploratory endpoints will be summarized descriptively. Tertiary endpoints of localization time, insertion time, and number of bone contacts will also be evaluated for homogeneity of the group results using a Mann-Whitney test. The exploratory endpoint of procedure time will also be evaluated with a Mann-Whitney test. The tertiary, safety, and exploratory incidence endpoints will be evaluated for homogeneity of the rates across the treatment groups using likelihood ratio tests.

8.2.4 Safety Analyses

Adverse events will be summarized using the number and percentage of subjects with one or more events and well as the total count of events. Adverse events will be summarized overall, by device relatedness, seriousness, and severity. Adverse events will only be summarized descriptively.

9 Safety and Adverse Events

9.1 Definitions

Adverse Event (AE)

An adverse event (AE) is any symptom, sign, illness or experience that develops or worsens in severity during the course of the study. Intercurrent illnesses or injuries will be regarded as adverse events. Abnormal results of laboratory or diagnostic procedures are considered to be adverse events if the abnormality:

- Results in study withdrawal
- Is associated with a serious adverse event

- Is associated with clinical signs or symptoms
- Leads to additional treatment or to further diagnostic tests
- Is considered by the Investigator to be of clinical significance.

Serious Adverse Event (SAE)

A serious adverse event (SAE) is any adverse event that is:

- Fatal
- Life-threatening
- Requires or prolongs a hospital stay
- Results in persistent or significant disability or incapacity
- Necessitates medical or surgical intervention to prevent one of the outcomes listed above (i.e., to preclude permanent impairment of a body function or permanent damage to a body structure)
- A congenital anomaly or birth defect

Hospitalization

Hospitalization shall include any initial admission (even if less than 24 hours) to a healthcare facility as a result of a precipitating clinical adverse effect; to include transfer within the hospital to an intensive care unit. Hospitalization or prolongation of hospitalization in the absence of a precipitating, clinical adverse effect (e.g., for a preexisting condition not associated with a new adverse effect or with a worsening of the preexisting condition; or admission for a protocol-specified procedure) is not, in itself, a serious adverse effect.

Unanticipated Adverse Device Effect (UADE)

An unanticipated adverse device effect is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Adverse Event Relationships to the Study Device

The relationships between adverse events and the study device will be characterized by the definitions below.

- *Unrelated:* This category applies to those adverse events which, after careful consideration, are clearly and incontrovertibly due to extraneous causes (disease, environment, etc.)

- *Possibly Related:* This category applies to those adverse events for which, after careful medical consideration at the time they are evaluated, a connection with the study device administration appears unlikely but cannot be ruled out with certainty. An adverse experience may be considered possibly related if or when (at least two of the following):
    - It follows a reasonable temporal sequence from administration of the study device.
    - It could not readily have been produced by the subject's clinical state, environmental or toxic factors, or other modes of therapy administered to the subject.
    - It follows a known pattern of response to the study device.
- *Probably Related:* This category applies to those adverse events which, after careful medical consideration at the time they are evaluated, are believed with a high degree of certainty to be related to the study device. An adverse experience may be considered probably related if or when (at least three of the following):
    - It follows a reasonable temporal sequence from administration of the study device.
    - It could not be reasonably explained by the known characteristics of the subject's clinical state, environmental or toxic factors or other modes of therapy administered to the subject.
    - It disappears or decreases on cessation or reduction in device exposure. There are important exceptions when an adverse event does not disappear upon discontinuation of the device, yet device-relatedness clearly exists.
    - It follows a known pattern of response to the study device.
- *Definitely Related:* An adverse event may be considered definitely related if or when all of the following apply:
    - The event is a known effect of the device, or procedure
    - The event follows an obvious sequence of time, from the device's implantation or activation, or procedure, for which the event is directly attributed to the administration, implantation, activation, or procedure.
    - The event ceases with discontinuation of the device, or procedure (and reoccurs on restarting).

Device Malfunction/Failure – Device Specific Events

A device specific event (DSE) is any malfunction of the device, related or not to the device, resulting or not in the patient undergoing undesirable or harmful experience, that occurs in relation with the conduct of the study.

Device malfunction means the failure of a device to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed.

Device malfunction may or may not result in the subject experiencing a harmful effect.

All AEs/SAEs associated with a device failure are by definition device related.

9.2 Safety Monitoring Plan

Procedures for ensuring subject safety are addressed throughout this protocol, and a separate Data Safety Monitoring Plan will not be required. Any incidental findings associated with clinical procedures will be provided to the subject with a recommendation for follow-up with their primary physician. The site Principal Investigator, or designee, will serve as the Emergency Medical Safety Contact for subjects enrolled at that site.

9.2.1 Anticipated Risks / Risk Mitigation

As discussed, neuraxial procedures have long been associated with concerns of uncertainty and subjectivity. VerTouch is designed to integrate into the existing clinical workflow and environment; and to offer additional information in support of these procedures, with greater objectiveness than palpation, and greater interpretability than ultrasound.

IntuiTap has performed risk analyses in accordance with ISO 14971:2019, IEC 62366:2015, IEC 62304:2006, and IEC 60601-1, from which the following categories of anticipated VerTouch risks have been identified:

- Failure to support proper identification of an insertion site (e.g. generates scanning output that is not uniform, aligned, or sufficiently sensitive)
- Failure to support proper needle insertion (e.g. provides marker or needle guidance that is not accurate, precise, or intuitive)
- Tissue trauma (e.g. causes needle dragging, or excessive levels of sustained force)
- Standard risks associated with electromechanical medical devices (e.g. is not biocompatible, sterile, or electrically safe)

The first two categories could be associated with an increase in procedure time and/or an incorrect needle insertion. In nearly all indications, added time would not result in serious harm. If occurring in emergent cases, particularly in labor/delivery where the opportunity to administer anesthesia could be missed, the provider could revert to the manual procedure. In general, the consequence of an incorrect insertion associated with VerTouch would be identical to that with the standard of care. Namely, it would warrant reinsertions and/or redirections, which can be associated with certain adverse events that are possible in any neuraxial procedure, as listed in Section 9.3, most of which are very rare and/or have low prevalence. Among these, more severe harm exists in epidural and intrathecal injections, where incorrect insertion can result in incorrect administration of a drug or anesthetic.

All risks belonging to the above categories will be reduced as far as possible via safety by design, protective measures, and information for safety. To mitigate the risk of device failure, design verification will be completed, including bench, usability, and standards testing, prior to study execution. Labeling will be provided to ensure proper use of all VerTouch components.

As with the standard of care and the ultrasound alternative, IntuiTap has assessed the potential for risks in the above categories to be exacerbated by certain provider and/or patient characteristics. VerTouch formative and early IRB-approved testing, which has included residents (after their internship) through attendings, and non-MDs, has evidenced no significant difference in use errors and/or insertion performance associated with indicators of provider skill, such as provider level of training or experience with neuraxial procedures. However, to protect the direct risk to subjects, all Investigators will receive the same training on the use of the device and on study procedures, and must be approved by IntuiTap prior to enrollment. Training will follow a checklist that aligns with the IFU, and will include hands-on interaction with the Device. With regard to patient characteristics, formative testing has evidenced some challenges associated with using the Device in simulated patients with high BMI and/or in the lateral-decubitus position, but none that significantly impacted insertion performance. To mitigate these, the indications and instructions for use have been refined to ensure safe and effective Device use across indicated patients; and training will include simulated use in representative challenging cases.

IntuiTap has also assessed and mitigated potential risks associated with the Device being left in place during needle insertion. For example, with an earlier version of the Device, there was a potential concern that while the

Device is still in place, it could obstruct the lumbar anatomy, precluding users from being able to confirm that their identified insertion site is aligned with the midline and at a safe vertebral level before they advance the needle at that site, possibly so deeply as to injure critical structures. This risk has been mitigated by the design and incorporation of the earlier-described Restrictor in the current Device, which limits the possible travel of an introducer or needle placed through the Device to a depth at which it is both safe and secure. After this depth is reached, the Device must be removed from the introducer or needle, such that the user has an unobstructed visualization of the insertion site before he/she continues advancing the needle. Section 9.2.1.1 details the evolution of the Restrictor. IntuiTap has also identified and mitigated any lower-level contributors to potential concerns about the Device being left in place during insertion. Among these are design specifications (and verification to these specifications) related to the level of stability and visibility when the device is in place; and the tolerance afforded to a needle during placement and Device removal. Importantly, the VerTouch IFU also includes an instruction for the use of standard landmarking techniques (i.e. palpation of the iliac crest) to identify a safe level for the procedure area prior to Device placement.

9.2.1.1 Restrictor Discussion

In the course of development, IntuiTap found that there are no anatomical structures in the region that are formally acknowledged as critical, and that needle depth has not been identified as an independent risk factor for any theoretical adverse events associated with placement of a spinal needle (such as retroperitoneal bleeding, epidural hematoma, and nerve root injury, identified in Section 9.3). However, in a conservative approach, IntuiTap designates a safe depth as within the posterior tissue shallower than the spinal landmarks, which includes skin, subcutaneous tissue, small blood vessels, and muscle, all of which are routinely pierced in neuraxial procedures, without significant and/or lasting damage[34-36]. The maximum depth is determined based on tissue thickness for the BMI expected with use of particular spinal needles, calculated using correlation coefficients provided by a study on spinal landmark depth[37]. Clinical users have expressed a desire for a minimum depth of 2.0cm or, alternatively, 30% of the needle shaft in order to feel that their introducer or needle is secure enough to remain in the tissue during Device removal.

Since most clinical participants in VerTouch testing have stated that they can determine a safe initial placement depth without the restrictor, based on training and skill in gauging needle depth by tissue consistency and resistance felt during placement, IntuiTap's intent was to address this safety objective with minimal complexity and impact on existing workflow. To that end, Restrictor configurations were defined for the most commonly used needles for these procedures: introducers (1.25"), and 3.5" and 5" spinal needles (the 5" are a rare alternative to the 3.5"; used only in cases of morbid obesity). The design of the existing Needle Guide reduces the penetrable depth of any needle by 2.0cm, which is what is needed to stop an introducer at the secure depth of 1.0cm. With the appropriate Restrictor configurations, the 3.5" and 5" needles can reach depths of 2.0cm and 3.5cm respectively, which fall within the safe and secure range established by the above discussion. In the event that a provider opts to use a 5" needle in lower-BMI cases, literature shows that it will still be prevented from reaching the epidural space, less conservatively allowing the needle to be placed through interspinous ligament, if BMI exceeds 20kg/m^2; likewise for a 3.5" needle in patients with less than 2.0cm subcutaneous tissue[11,38-40]. The Restrictor embodiment shown in Section 3.5 has been successfully tested in bench and usability studies. It is important to note that in this testing no significant difference has been observed in Device performance using the marking versus introducer or needle placement workflows (except where attributed to shortcomings in test methodology), despite the latter not enabling visual confirmation of the identified site until after the Device is removed.

9.2.2 Medical Monitoring for Participant Safety

The Principal Investigator will oversee the safety of the study, including careful assessment and appropriate reporting of adverse events as outlined in Section 9.4. Medical monitoring will include a regular assessment of the number and type of serious adverse events.

Medical Monitor:

ICON Clinical Research
888-723-9952 (Telephone)

9.3 Anticipated Adverse Events

Anticipated adverse events are outlined below, with control rates listed separately as reported in the literature on LPs and neuraxial anesthesia. Few adverse events are associated with insertion attempts, and with the exception of unintended dural puncture, none have been directly tied to insertion depth (if performed at the correct vertebral level, below the cauda equina). It is important to note that the various risk factors associated with nearly all of these complications lead to great variability in reported rates. In particular, the incidence of most adverse events that can be linked to number of insertion attempts is directly correlated with needle characteristics, such as size and shape[8]. Additionally, rare complications have been found to be associated with the presence of spinal deformities, which are study exclusions[34,35].

Adverse events associated with LPs include[41]:

- PDPH, 40% (important risk factors include needle size and shape, use of stylet, patient position, number of attempts, and volume of CSF removed; may lead to the need for further treatment, including epidural blood patch)[42]
- Cranial neuropathy, 0.4%
- Paresthesia (nerve root irritation), 13%[43]
- Low back pain, 35%
- Bacterial meningitis, 0.2%
- Intracranial bleeding, rare
- Traumatic lumbar puncture, up to 72%, with 15.6% reported for cutoff of 400 erythrocytes/μL in the first tube (in laboratory analysis, may lead to false-positive diagnosis of SAH or other cerebral vascular malformations)[43,44]
- Retroperitoneal abscess, rare[45]
- Spinal hematoma, rare

Adverse events associated with neuraxial anesthesia include the following (rates are mostly reported for epidural anesthesia; where not specific to an epidural, rates are higher with spinal and combined spinal-epidural anesthesia)[46,47]:

- Unintended dural puncture, 1.5%
- Post-dural puncture headache, 0.21-1.5%
- Spinal abscess, 0.0002%
- High spinal block, 0.002%
- Paresthesia (transient neurologic injury), 0.018%[9]
- Spinal hematoma, 0.0002%

- Hypotension (requiring treatment), 30%
- Persistent neurologic injury, 0.0004%[9]
- Permanent neurological injury, 0.001%
- Inadequate analgesic effect (failure), 6.3%
- Pruritus, 12%
- Backache, 12%
- Nerve damage caused by needle trauma, 0.0006%
- Epidural abscess, 0.003%
- Bacterial meningitis, 0.003%
- Epidural hematoma, 0.0006%
- Fetal heart rate abnormalities: 5.5%
- Fetal bradycardia: 4.7%

9.4 Adverse Event Reporting

All Adverse Events occurring during the study period must be recorded. The clinical course of each event will be followed until resolution or stabilization, or until it has been determined that study treatment or participation is not the cause.

The Investigator will promptly review documented adverse effects and abnormal test findings to determine:

1) if the abnormal test finding should be classified as an adverse effect;
2) if there is a reasonable possibility that the adverse effect was caused by the investigational device or, if applicable, other study treatment or diagnostic product(s); and
3) if the adverse effect meets the criteria for a serious adverse effect.

If the Investigator's final determination of causality is "unknown and of questionable relationship to the investigational device or, if applicable, other study treatment or diagnostic product(s)", the adverse effect will be classified as *associated with the use of the investigational device* for reporting purposes. If the investigator's final determination of causality is "unknown but not related to the investigational device or, if applicable, other study treatment or diagnostic product(s)", this determination and the rationale for the determination will be documented in the respective subject's case history.

9.4.1 Adverse Events

All observed or volunteered adverse effects and abnormal test findings, regardless of treatment group, if applicable, or suspected causal relationship to the investigational device or, if applicable, other study treatment or

diagnostic product(s) will be recorded in the subjects' case histories. For all adverse effects, sufficient information will be pursued and/or obtained so as to permit:

1) an adequate determination of the outcome of the effect (i.e., whether the effect should be classified as a serious adverse effect) and;

2) an assessment of the casual relationship between the adverse effect and the investigational device or, if applicable, the other study treatment or diagnostic product(s).

Adverse effects or abnormal test findings felt to be associated with the investigational device or, if applicable, other study treatment or diagnostic product(s) will be followed until the effect (or its sequelae) or the abnormal test finding resolves or stabilizes at an acceptable level.

Adverse Events that do not qualify as Serious Adverse Events, or as Unanticipated Adverse Device Effects will be reported to the Sponsor at a designated interval determined by the Sponsor.

Adverse Events that do not qualify as Serious Adverse Events, or as Unanticipated Adverse Device Effects will be reported to the IRB with the continuing review progress report.

9.4.2 Serious Adverse Events

Investigators must report serious adverse events to the Study Sponsor or designee within 24 hours of learning of the event. A serious adverse event form must be completed by the Investigator and communicated to the Study Sponsor within 24 hours. Study Sponsor contact information for Serious Adverse Event Notification:

ICON Clinical Research
888-723-9952 (Telephone)

At the time of the initial report, the following information should be provided:

- Study Identifier
- Study Center
- Subject Number
- Event Description
- Date of Onset
- Whether study treatment was discontinued
- Reason the event is classified as serious
- Investigator assessment of association between event and study device
- Current Status

Serious Adverse Events that are at least possibly related must be reported to the IRB within 10 working days.

9.4.3 Unanticipated Adverse Device Effects (UADE)

Investigators are required to submit a report of a UADE to the Sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the Investigator first learns of the event.

Sponsors must immediately conduct an evaluation of a UADE and must report the results of the evaluation to FDA, all reviewing IRBs, and participating Investigators within 10 working days after the Sponsor first receives notice of the effect.

If the Adverse Event is Serious, Unanticipated, Device Related, and determined by the Sponsor to present an unreasonable risk to subjects, the Sponsor must terminate the study within 5 working days of that determination, and not later than 15 working days after the sponsor first received notice of the effect.

10 Classification as Non-Significant Risk Study

The US Food and Drug Administration (FDA) has determined that the study may proceed under the non-significant risk (NSR) provisions of the IDE regulation.

The rationale for the NSR classification of this study is that the investigational Device does not meet the definition of a significant risk (SR) device under 21 CFR 812.3(m), as further described below:

- The Device is not an implant, nor does it present a potential for serious risk to the health safety, or welfare of a subject (812.3(m)(1));
- The Device is not purported or represented to be for a use in supporting or sustaining human life, nor does it present a potential for serious risk to the health, safety, or welfare of a subject (812.3(m)(2));
- The Device is not for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health, nor does it present a potential for serious risk to the health, safety, or welfare of a subject (812.3(m)(3)); and
- The Device does not otherwise present a potential for serious risk to the health, safety, or welfare of a subject (812.3(m)(4)).

As described in Section 9.2.1, the design of the Device and the procedures required by this protocol comprehensively mitigate and minimize potential risks to study subjects. Accordingly, the study is appropriately classified as an NSR study. As noted above, FDA has determined that the study may proceed under the NSR provisions of the IDE regulation without submission of an IDE application to FDA.

11 Data Handling and Record Keeping

11.1 Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

11.2 Source Documents

Source Data are the clinical findings and observations, laboratory and test data, and other information contained in *Source Documents*. *Source Documents* are the original records (and certified copies of original records); including, but not limited to, hospital medical records, physician or office charts, physician or nursing notes, subject diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, x-rays, etc. When applicable, information recorded on the CRF shall match the *Source Data* recorded on the *Source Documents*.

11.3 Case Report Forms

The study case report form (CRF) is the primary data collection instrument for the study. All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, enter "N/D". If the item is not applicable to the individual case, enter "N/A".

An electronic Case Report Form will be completed for each subject enrolled into the clinical study. All electronic records will be compliant to 21 CFR Part 11. The investigator will review, approve and sign/date each completed CRF; the investigator's signature serving as attestation of the investigator's responsibility for ensuring that all clinical and laboratory data entered on the CRF are complete, accurate and authentic.

11.4 Clinical Reports

An annual progress report will be submitted to the IRB by participating Investigators. Investigators will submit a final report of the clinical study to the sponsor and reviewing IRB within 3 months of termination or completion of the clinical study or the Investigator's part of the clinical study.

Sponsors will notify the FDA within 30 working days of the termination or completion of a significant risk clinical study. Sponsors will submit a final report to FDA, all reviewing IRBs and participating Investigators within 6 months of termination or completion. In the case of a non-significant risk study, the Sponsor shall submit a final report to all reviewing IRBs within 6 months after termination or completion.

11.5 Records Retention

The investigator will retain the specified records and reports for a minimum of 6 years, or up to 2 years after the marketing application is approved for the investigational device; or, if a marketing application is not submitted or approved for the investigational device, until 2 years after investigations have been discontinued, whichever is longer. The Investigator will provide the Sponsor with written notice no less than 30 days prior to any scheduled destruction of records.

12 Study Monitoring, Auditing, and Inspecting

This study will be monitored according to FDA/GCP guidelines. The Investigator will allocate adequate time for such monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to all

study-related documents and study related facilities (e.g. pharmacy, diagnostic laboratory, etc.), and has adequate space to conduct the monitoring visit.

12.1 Study Monitoring Plan

ICON will conduct monitoring visits at study initiation, study completion, and during the study as required. During these visits the monitor/s will review all aspects of the study to ensure that the protocol and applicable regulatory requirements and ISO 14155:2020 standard are adhered to. Monitoring activities will include checking CRFs and verifying data against source documentation, reviewing ICFs, checking the Device Accountability Log, and ensuring that the Site Study File is up to date and contains all the required documentation. ICON CRAs will contact sites regularly to ensure continuous oversight of study processes and follow-up on action items. Independent monitoring of the clinical study for clinical protocol compliance will be conducted periodically by qualified staff. In consideration of COVID-19 pandemic issues, where possible/feasible, remote source data verification, remote monitoring and remote investigational site closure visits may be employed.

12.2 Auditing and Inspection

The investigator will permit study-related monitoring, audits, and inspections by the IRB, the sponsor, government regulatory bodies, and institutional compliance and quality assurance groups of all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data, etc.). The investigator will ensure the capability for inspections of applicable study-related facilities (e.g. pharmacy, diagnostic laboratory, etc.).

Participation as an investigator in this study implies acceptance of potential inspection by government regulatory authorities and applicable institutional compliance and quality assurance offices.

13 Administrative Study Information

13.1 Technical Support

In the event of a device malfunction, the Sponsor contact is Geoffrey Hutchins, Director of Engineering. He can be reached at 847-916-7074 during normal business hours, Central Time. Outside of these hours, a new device can be used until the Sponsor contact can be reached.

13.2 Pre-Study Site Qualification

The Investigator must be of good standing as an Investigator and knowledgeable in relevant areas of clinical research to ensure adherence to the requirements of the protocol, including the protection of human subjects. Other site personnel must have appropriate research experience and infrastructure to ensure adherence to the protocol and enrollment of sufficient numbers of evaluable subjects. The curriculum vitae (CV) of the Investigator will be maintained in the Sponsor files as documentation of previous medical training, and federal databases will be searched to ensure that the Investigator and/or the site are not prohibited from engaging in federally Sponsored clinical research. The Principal Investigator will sign the signature page of this protocol, agreeing to comply with all applicable government regulations and the requirements of this study.

13.3 Protocol Amendments After Study Initiation

Should changes in the study plan or protocol become necessary in the course of the clinical trial, those specific changes will be discussed and agreed upon by the Sponsor, its acting representative if appropriate, Investigator, and appropriate IRB approval obtained before the changes are implemented. All changes must be documented as protocol amendments. For studies conducted under an IDE, FDA approval and/or notification may be required in addition to the IRB approval.

13.4 Materials / Services Provided by Sponsor and Coordinating Center

The Sponsor will provide the following materials and services:

- VerTouch reusable and disposable components
- Technical support as defined in Section 12.1 above
- A dedicated PC laptop for study data (if necessary)

14 Ethical Considerations

This study is to be conducted according to US and international standards of Good Clinical Practice, applicable government regulations (21 CFR 50, 54, 56 and 812) and Institutional research policies and procedures.

This protocol and any amendments will be submitted to a properly constituted independent Institutional Review Board (IRB), in agreement with local legal prescriptions, for formal approval of the study conduct. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator and a copy of this decision will be provided to the sponsor before commencement of this study.

15 Study Finances

15.1 Funding Source

This study is funded by IntuiTap Medical, Inc.

15.2 Conflicts of Interest

Conflicts of interest or perceived conflicts of interest will be addressed in accordance with the policies of the participating institutions. The Sponsor will maintain Investigator Financial Statements as required by 21 CFR 54.

16 Publication Plan

Neither the complete nor any part of the results of the study carried out under this protocol, nor any of the information provided by the sponsor for the purposes of performing the study, will be published or passed on to any third party without the consent of the study sponsor. Any investigator involved with this study is obligated to provide the sponsor with complete test results and all data derived from the study.

17 References

1. Hall, M.J., DeFrances, C.J., Williams, S.N., Golosinskiy, A., & Schwartzman, A. (2010). National hospital discharge survey: 2007 summary. *National Health Statistics Report*, 29.
2. Osterman, M.J.K. & Martin, J.A. (2011). Epidural and spinal anesthesia use during labor: 27-state reporting area, 2008. *National Vital Statistics Report*, 59(5).
3. Orthoworld (2012). Orthopaedic industry annual report: focus on joint replacement. *Orthoknow*. Retrieved from: https://www.orthoworld.com/index.php/fileproc/index/knowentADJADJorthoknowADJADJ2012ADJADJorthoknow1206LXLXLXpdf
4. Manchikanti, L., Falco, F.J.E., Singh, V., Pampati, V., Parr, A.T., Benyamin, R.M., Hirsch, J.A. (2012). Utilization of Interventional techniques in managing chronic pain in the Medicare population: analysis of growth patterns from 2000 to 2011. *Pain Physician*, 15(6), E969-E982.
5. Robbins, E., & Hauser, S.L. (2015). Technique of lumbar puncture. In Kasper, D., Fauci, A.S., Hauser, S.L., Longo, D.L., Jameson, J.L., & Loscalzo, J. (Eds.), *Harrison's principles of internal medicine* (19th ed). New York, NY: McGraw-Hill.
6. Farley, A., & McLafferty, E. (2008). Lumbar puncture. *Nursing standard*, 22(22). 46-48.
7. Bhattacharjee, S., & Kauer, G. (2013). A study on the standard of documentation of lumbar puncture in neurology department of a major Irish Teaching Hospital in Ireland. *Annals of Indian Academy of Neurology*, 16(4), 627-630.

8. Tung, C.E., So, Y.T., & Lansberg, M.G. (2012). Cost comparison between the atraumatic and cutting lumbar-puncture needles. *Neurology*, 78(2), 109-113.
9. Ruppen, W., Derry, S., McQuay, H., & Moore, A. (2006). Incidence of epidural hematoma, infection, and neurologic injury in obstetric patients with epidural analgesia/anesthesia. *Anesthesiology*, 105(2), 394-399.
10. Cook, T.M., Counsell, D., & Wildsmith, J.A.W. (2009). Major complications of central neuraxial block: report on the Third National Audit Project of the Royal College of Anaesthetists. *British Journal of Anaesthesia*, 102(2), 179-190.
11. Halpenny, D., O'Sullivan, K., & Burke, J.P., & Torreggiani, W.C. (2013). Does obesity preclude lumbar puncture with a standard spinal needle? The use of computed tomography to measure the skin to lumbar subarachnoid space distance in the general hospital population. *European Radiology*, 23(11), 3191-3196.
12. Fryar, C.D., Carroll, M.D., & Ogden, C.L. (2016). Prevalence of overweight, obesity, and extreme obesity among adults aged 20 and over: United States, trends 1960-1962 through 2013-2014. *NCHS Health E-Stat*. Retrieved from: https://www.cdc.gov/nchs/data/hestat/obesity_adult_13_14/obesity_adult_13_14.htm
13. Kroll, H., et al (2015). Trends in lumbar puncture over 2 decades: a dramatic shift to radiology. *American Journal of Roentgenology*, 204, 15-19.
14. The Joint Commission (2011). Radiation risks in diagnostic imaging. *Sentinel Event Alert*, 47. Retrieved from: https://www.wvdhhr.org/rtia/pdf/SEA_47[1].pdf
15. Menger, R.P., Peyton, W.A., Hefner, M., Nanda, A, Cuellar, H. (2017). Economic outcomes of the addition of fluoroscopic guidance to the lumbar puncture procedure: a call for standardized training. *Journal of Spine*, 6(1).
16. Gaskin, D.J., & Richard, P. (2012). The economic costs of pain in the United States. *The Journal of Pain*, 13(8), 715-724.
17. Furness, G., Reilly, M.P., & Kuchi, S. (2002). An evaluation of ultrasound imaging for identification of lumbar intervertebral level. *Anaesthesia*, 57(3), 277-280.
18. Dahiya, R.S., & Valle, M. (2013). Tactile sensing: definitions and classification. In Dahiya, R.S., & Valle, M. (Eds.), *Robotic tactile sensing: technologies and system*. Dordrecht, Netherlands: Springer.
19. Pines, J.M., Batt, R.J., Hilton, J.A., & Terwiesch, C. (2010). The financial consequences of lost demand and reducing boarding in hospital emergency departments. *Annals of Emergency Medicine*, 58(4), 331-340.
20. Nicks, B.A., & Manthey, D.M. (2012). The impact of psychiatric patient boarding in emergency departments. *Emergency Medicine International*, 2012.
21. Falvo, T., Grove, L., Stachura, R., Vega, D., Stike, R., Schlenker, M., & Zirkin, W. (2007). The opportunity loss of boarding admitted patients in the emergency department. *Academic Emergency Medicine*, 14(4), 332-337.
22. Moskowitz, N.C., Traver, J., Garcia-Rojas, X., & Ganjeh, Y. (2018). US10004450B2: tactile sensing device for lumbar punctures. *USPTO*.
23. Moskowitz, N.C., Traver, J., Garcia-Rojas, X., Ganjeh, Y., Cruz, M., Plumb, J.R., Lowe, J.A., & Jones, A.K.G.P (2019). US10383610B2: Tactile sensing and needle guidance device. *USPTO*.
24. VerTouch™ Instructions for Use, available upon request.

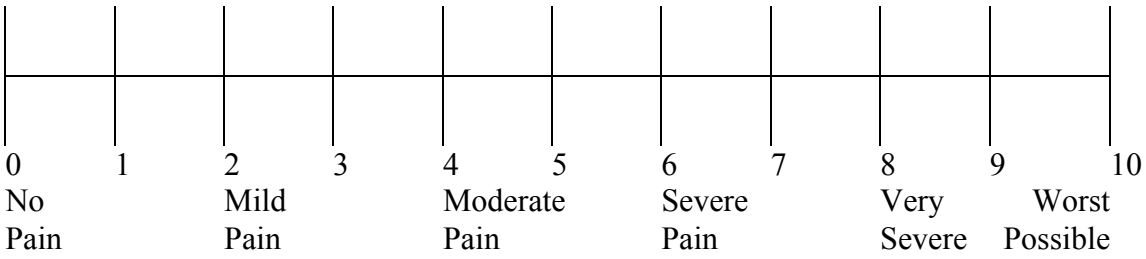
25. Chin, KJ, Perlas, A, Chan, V, Brown-Shreves, D, Koshkin, A, & Vaishnav, V (2011). Ultrasound imaging facilitates spinal anesthesia in adults with difficult surface anatomic landmarks. *Anesthesiology*, 115(1), 94-101.
26. Cho, YC, Koo, DH, Oh, SK, Jeong, WJ, Lee, WS, You, YU, & Yoo, IS (2009). Comparison of ultrasound-assisted lumbar punctures with lumbar puncture using palpation of landmarks in aged patients in an emergency center. *Journal of Korean Society of Emergency Medicine*, 20(3), 304-309.
27. Grau, T, Leipold, RW, Conradi, R, Martin, E, & Motsch, J (2002). Efficacy of ultrasound imaging in obstetric epidural anesthesia. *Journal of Clinical Anesthesia*, 14(1), 169-175.
28. Lee, WS, Jeong, WJ, Yi, HY, Ryu, S, Lee, JW, & Kim, SW (2008). The usefulness of ultrasound-assisted lumbar puncture on adult patients in the emergency center: comparison with classic lumbar puncture. *Journal of Korean Society of Emergency Medicine*, 19(1), 562.
29. Mofidi, M, Mohammadi, M, Saidi, H, Kianmehr, N, Ghasemi, A, Hafezimoghadam, P, & Rezai, M (2013). Ultrasound guided lumbar puncture in emergency department: time saving and less complications. *Journal of Research in Medical Sciences*, 18(4), 303-307.
30. Nomura, JT, Leech, SJ, Shenbagamurthi, S, Sierzenski, PR, O'Connor, RE, Bollinger, M, & Gukhool, JA (2007). *Journal of Ultrasound Medicine*, 26(1), 1341-1348.
31. Peterson, MA, Pisupati, D, Heyming, TW, Abele, JA, & Lewis, RJ (2014). Ultrasound for routine lumbar puncture. *Academic Emergency Medicine*, 21(1), 130-136.
32. Singla, P, Dixon, AJ, Sheeran, JL, Scalzo, D, Mauldin, FW & Tiouririne, M (2019). Feasibility of spinal anesthesia placement using automated interpretation of lumbar ultrasound images: a prospective randomized controlled trial. *Journal of Anesthesia & Clinical Research*, 10(2).
33. Wan, X., Wang, W., Liu, J, & Tong, T (2014). Estimating the sample mean and standard deviation from the sample size, median, range, and/or interquartile range. *BMC Medical Research Methodology*, 14(135). Retrieved from: https://bmcmedresmethodol.biomedcentral.com/track/pdf/10.1186/1471-2288-14-135
34. Bruha, R, & Simon, S (1999). Lumbar puncture complicated by retroperitoneal hemorrhage. *Am J Medicine*, 107.
35. Aveline, C, & Bonnet, F (2004). Delayed retroperitoneal haematoma after failed lumbar plexus block. *Br J of Anaesthesia*, 93(4).
36. Myers, M, Meyers, L, & Fink, WA (2015). Extensive subarachnoid and epidural hematoma after lumbar puncture. *Am J Emergency Medicine*, 33.
37. Kawchuk, GN, et al (2011). Spinal landmark depth in relation to body mass index. *Manual Therapy*, 16.
38. Ravi, KK, et al (2011). Distance from skin to epidural space: correlation with body mass index (BMI). *Journal of Anaesthesiology Clinical Pharmacology*, 27.
39. Hoffmann, VLH, et al (1999). Posterior epidural space depth: safety of the loss of resistance and hanging drop techniques. *British Journal of Anaesthesia*, 83(5).

40. Westbrook, JL, et al (1993). Study of the anatomy of the extradural region using magnetic resonance imaging. *British Journal of Anesthesia*, 71.
41. Evans, RW (1998). Complications of lumbar puncture. *Neurologic clinics of North America*, 16(1).
42. Frank, RL (2008). Lumbar puncture and post-dural puncture headaches: implications for the emergency physician. *The Journal of Emergency Medicine*, 35(2).
43. Eskey, CJ and Ogilvy, CS (2001). Fluoroscopy-guided lumbar puncture: decreased frequency of traumatic tap and implications for the assessment of CT-negative acute subarachnoid hemorrhage. *American Journal of Neuroradiology*, 22.
44. Shah, KH, Richard, KM, Nicholas, S, and Edlow, JA (2003). Incidence of traumatic lumbar puncture. *Academic Emergency Medicine*, 10(2): 151-154.
45. Boon, JM, Abrahams, PH, Meiring, JH, and Welch, T (2004). Lumbar puncture: anatomical review of a clinical skill. *Clinical Anatomy*, 17(1): 544-553.
46. Huang, C and Macario, A (2002). Economic considerations related to providing adequate pain relief for women in labour. *Pharmacoeconomics*, 20(5).
47. Silva, M and Halpern, SH (2010). Epidural analgesia for labor: current techniques. *Local and Regional Anesthesia*, 3.

18 Appendices and Attachments

18.1 Subject Discomfort During Landmarking

Subject discomfort will be assessed using a VAS as below. The scale is to be a total of 100 mm from 0 to 10.



18.2 Provider Confidence

Provider confidence in the identified insertion site will be assessed using a Likert scale as below. This scale is to be a total of 100 mm from 1 to 5.