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3D Ultrasound-guided Labor Epidural Analgesia in the Morbid Obese Parturient: A Randomized Control Trial

Principal Investigators
Rovnat Babazade, MD

Co-investigators
George Saade, MD
Rakesh B. Vadhera, MD
Antonio Saad, MD
Michelle Simon, MD
Denise M. Wilkes, MD

Departments of Anesthesiology and Obstetrics and Gynecology
The University of Texas Medical Branch (UTMB) at Galveston

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1. **Introduction/Background/Purpose:**

Worldwide obesity has become an epidemic. The obstetrical population is no exception [1]. This made more challenging for anesthesiologists on labor and delivery units to administer epidural analgesia [2, 3]. According to the World Health Organization, more than 30% of U.S. adults are obese with a body mass index (BMI; in kg/m^2) ≥ 30 [4]. It has been reported that more than half of the obstetrical population is overweight or obese [6, 7]. Obesity has been associated with serious co-morbidities linked to poor maternal and fetal outcomes, such as gestational hypertension/preeclampsia, gestational diabetes, and increased maternal mortality [7-9]. Obese mothers have a higher risk of undergoing cesarean delivery and operative vaginal deliveries, thus underlining the importance of obtaining an effective neuraxial anesthesia [1 - 3] [9]. General anesthesia in the obese parturient involves risks such as difficult airway, aspiration pneumonitis and failed resuscitation from hemodynamic collapse [7] [10] [11]. Recent data has shown that increased BMI has been associated with increased neuraxial analgesic failure and difficulty with prolonged epidural placement time [12].

The 'Blind approach' is the current standard of care in administering neuraxial anesthesia. The physician palpates the patient's spinal bony landmarks; the needle is placed in relation to identified landmarks and inserted until loss of resistance is felt. In the obese population the success rates is as low as 68% [12]. Recently the FDA has approved a handheld device "The Accuro" as an adjunct for neuraxial analgesia (Rivanna Medical, LLC). It consists of a three-dimensional ultrasound device. By utilizing sound waves it constructs three-dimensional images of the spinal column, allowing the physician to better see the spine in order to perform spinal/epidural anesthesia. The device is a pocket-sized and battery operated ultrasound instrument that incorporates new signal processing-based technologies for enhanced bone imaging including 3D navigation of the lumbar spine *(Figure 1).* The device is a single self-contained unit consisting of an ultrasound system, ultrasound probe, and rotatable touchscreen

display. The instrument enables a SpineView3D™ technology to facilitate spinal anesthesia guidance with real-time 3D navigation of the lumbar spine anatomy. SpineView3D™ technology facilitates image interpretation of individual 2D lumbar spine scans by automating spinal bone landmark detection and depth measurements and providing a real-time assessment of scan plane orientation in 3D. SpineView3D™ makes image interpretation and measurements of the lumbar spine anatomy simple, quick, and easy *(Figure 2).* Real-time 2D scans from either SpineView3D™ or general-purpose bone presets are formed using patent-pending BoneEnhance+™ technology. The BoneEnhance+™ technology provides images of bone anatomy at greater bone-to-tissue contrast compared with conventional ultrasound image reconstructions. We hypothesize that this device will enable clinicians to assess epidural spaces for epidural needle placement compared with the traditional Blind approach in the morbid obese parturient.

This study will be an open label randomized control study, with the objective to evaluate epidural analgesia success rates between the two methods (Blind Approach versus Accuro Device). Also, will determine if ultrasound based landmarks would reduce the needle tract and thereby reduced the amount of post-procedure pain at the insertion site in the peripartum period by using the algometer.

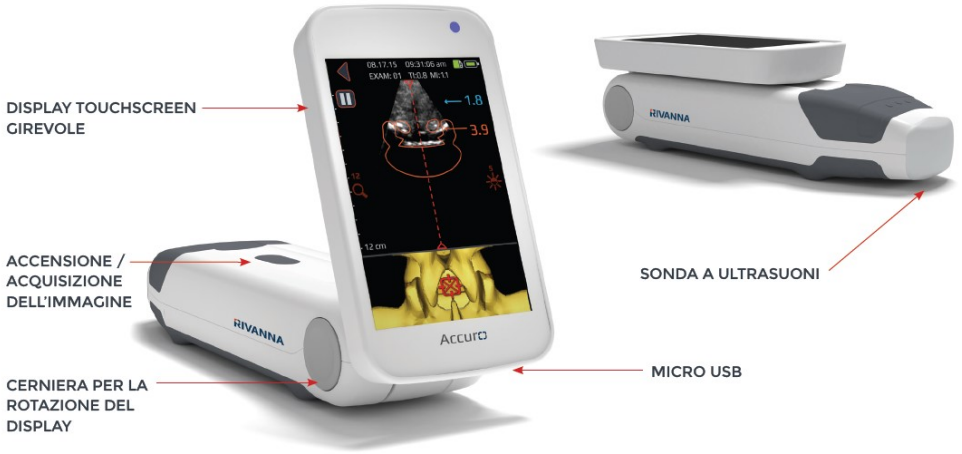

Figure 1. "The Accuro" 3D ultrasound

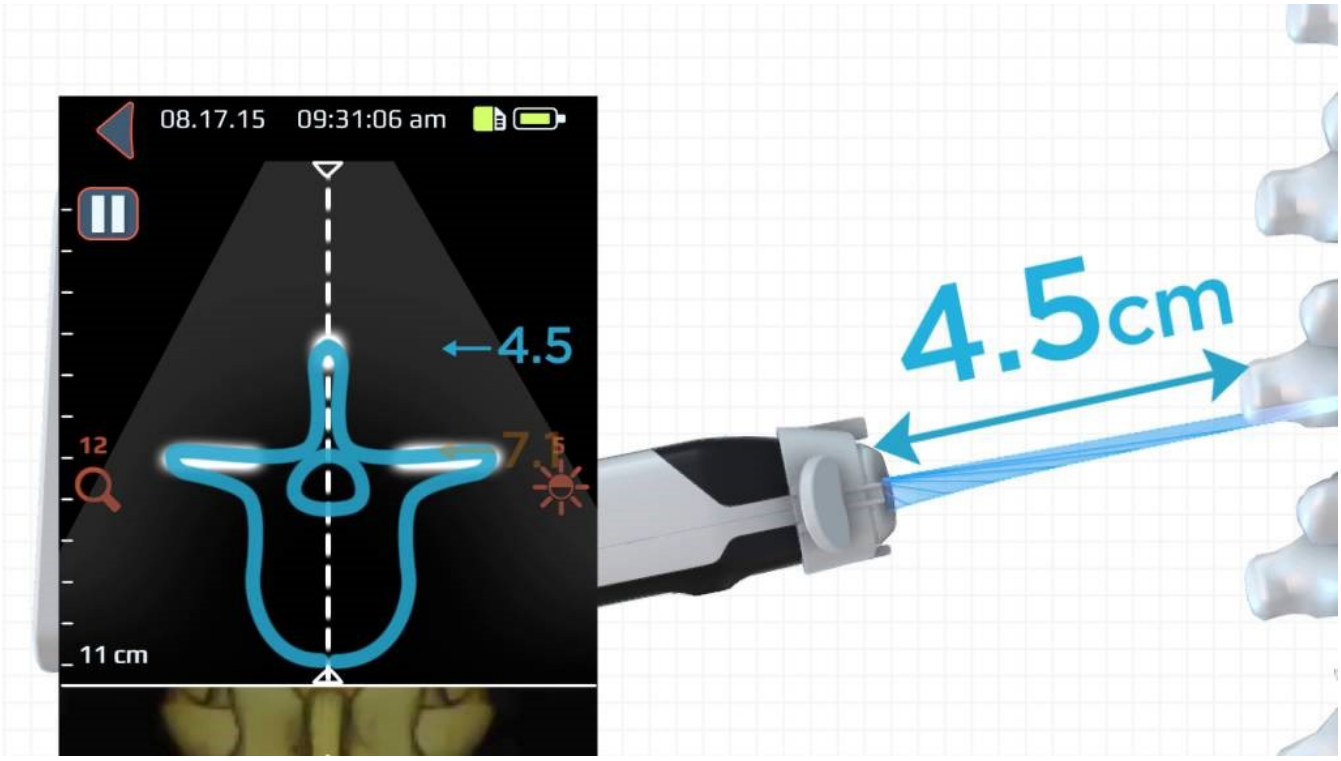

Figure 2

2. **Concise summary of project:**

This will be an open label randomized control study. All women requesting labor epidural analgesia will be approached for participation in labor and delivery private room at same day of admission. **If eligibility criteria of the study** are met, written informed consent will be obtained from patients by the primary investigator (PI), study coordinator, or designated collaborators. After informed consent is obtained, the subject will be randomized to the study group (Ultrasound; Accuro) or the control group (blind technique).

The **treatment group (Group 1: Ultrasound and Epidural)** will receive epidural analgesia using ultrasound pre-procedural scan with the ACCURO ™ device. The anesthesiologist will perform a pre-procedural lumbar spine scan to detect the needle entry site. After image optimization, the Accuro probe will be aligned with the spine

mid-line, as indicated by a dashed redline on the screen. After that the interlaminar space at the desired intervertebral level will be detected, as indicated by orange overlay in the screen. The depth and the device angle used to detect the interlaminar space will be annotated. The anesthesiologist will then disengage the Accuro Locator needle guide and press gently against the skin. Then the probe will be removed and the epidural catheter will be placed.*(Figure 3)*

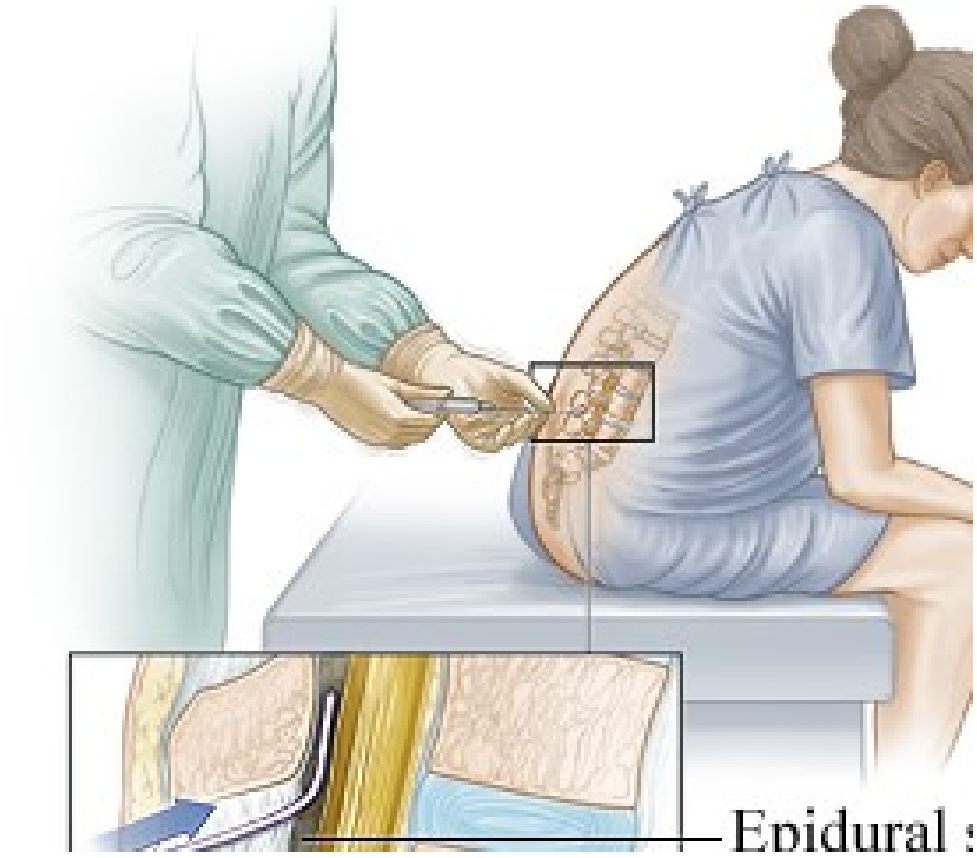

Figure 3. Epidural catheter placment

The **control group (Group 2: Epidural)** will receive the 'Blind/standard approach', which is the current standard of care using palpation in administering labor epidural analgesia. Additionally, anesthesiologist will scan patient's back with Accuro device in turned off mode.

The anesthesiologist will identify lumbar spinous processes with traditional landmark palpation. Once the correct interspinous level and the mid-line are identified, the anesthesiologist will proceed with needle insertion and epidural catheter placement.

Patients in both groups will undergo:

I. Standard monitoring with Non Invasive Blood Pressure (NIBP) cuff, Pulse-oximetry (SpO2) and fetal monitoring.
II. Peripheral intravenous access
III. Epidural analgesia performed by anesthesiologists (residents and staff) skilled in both techniques (conventional landmark technique or Accuro guided) at the L3-L4, L4-L5 or L5-S1 level, with a 17 gauge thouy needle.
IV. In both groups an observer will monitor and register epidural procedure duration (starting point: anesthesiologist wearing sterile gloves, ending point: fixing and taping epidural catheter).
V. Procedural difficulty will be rated by the performing anesthesiologist on a 10-point Likert scale from one (easy) to ten (extremely difficult).

Pressure pain thresholds

In both groups Pressure pain thresholds (PPT) will be obtained immediately prior to the epidural placement. The force that the patient will be indicated uncomfortable will be recorded. Each intervertebral level will be measured once. The PPT will be measured the next day after the discontinuation of the epidural. Back pain will be defined as a 20% decrease in PPT in at least one level. An algometer (Wagner FPXTM, Greenwich CT) will be used to test the sensitivity at each of those marked spots. The algometer worked by applying an increasing amount of pressure up to 60 Newton's (N). If the subject felt discomfort before 60N will be reached, they would notify the researcher and the force will be recorded.

In both groups, the resident administering the epidural will inform the research team when a bony contact will be made. The research team would also observe and record the number of redirections, reinsertions, and instances when they will be unable to thread the catheter. A redirection will be defined as any movement where the tuohy will be retracted. Reinsertions will be defined as a new skin insertion.

No significant direct adverse effects are expected with the use of the device in the study population since it is noninvasive. Please refer to below to section 8.3 for expected adverse effects/ risks for epidural catheter placement.

The study period will be between January 1, 2018, and January 1, 2020. The number of subjects studied will be 308 subjects at UTMB.

The subject will be withdrawn from the study if she wishes to discontinue participation. Demographic information will be obtained from the electronic medical record. Measured variables will include personal and obstetric data (age, height, weight), number of pregnancies, parity, failed epidural rate, epidural insertion attempts, staff interventions (need for the attending anesthesiologist assistance during the placement attempt), number of epidural top ups required, accidental dural puncture (ADP) rate, maternal delivery outcome.

The data will be kept on a password secured UTMB computer. An encrypted USB flash drive will be used to transfer data. The data will be identified and linked to the patient using the medical record number (MRN). During data analysis, all patient identifiers will be deleted.

3. Study procedures:

The decision to proceed with epidural analgesia will be taken by the managing clinical team and subject independent of the trial. After a subject who meets inclusion criteria

agrees to participation in our study, the obstetric team will contact one of the investigators. Signed informed consent will be obtained by the PI, study coordinator, or collaborators. The total participation time in the study will be up to discharge home from hospital.

The data collected will be kept on a password-secured UTMB computer. An encrypted USB flash drive will be used to transfer data. The data will be linked to the subject by subject's MRN number. This identifier is needed to access and analyze demographic data. During analysis of the data, all identifiers will be deleted.

A total of two study visits will be encountered throughout the study:

VISIT#1

3.1 Screening, Recruitment and Consenting:

Under the direction of the PI, trained research staff will be available 24/7 to **screen** and **consent** subjects according to study protocol. Potential subjects on L&D will be informed about the study but will not be consented or randomized until a decision for epidural analgesia is taken by the clinical team.

Whenever practical and feasible, information about our research project will be made available to patients prior to labor. In other words, we will inform patients of the study when they come to labor and delivery. We will not consent patients who appear not to be able to evaluate their options (such as recent iv narcotics).

After informed consent is obtained, the subject will be randomized to the Ultrasound group or the control group. A screening log will be used to track all subjects approached for the study. Women will only be randomized on L&D when the decision is made to do an epidural analgesia AND they continue to be eligible.

- Recruitment: We will recruit all pregnant subjects admitted to L&D for delivery who will be receiving epidural analgesia during the course of labor or before

cesarean delivery. Once the inclusion criteria for our study are met, the clinical team will inform the subject about the study and ask her authorization to contact one of the study personnel.

- Consenting process: Written consent will be obtained by direct person-to-person contact. The principal investigator, study coordinator, or a collaborator will be responsible for the informed consent. Spanish speaking subjects are anticipated to be part of the study population and informed consent will be provided in their primary language.

The data collected will not be used for clinical diagnosis or treatment purposes.

Subjects will be reassured that participation in the study is voluntary and will not interfere with diagnosis or treatment of her condition.

The subjects will receive the same care and expertise as any other subject treated in our unit.

3.2 Randomization and Masking:

A confidential computer-generated simple randomization scheme (using STATA 14, Dallas, TX) will be prepared and provided to our study coordinator. A randomization log with group assignment, subject name and medical record number will be used to track the randomization process.

3.3 Device guided placement of epidural catheter:

Because ultrasound visualization is dependent on the skill of the user, all ultrasound examinations will be performed by the anesthesia residents/attending who had performed at least 20 successful procedures with the ultrasound-guided epidural catheter placements before initiation of the study.

VISIT#2

At 24 hours postpartum, our research staff will be assessing parturient satisfaction with analgesia during labor using the Numerical Rating Scale (NRS) pain score described below and epidural analgesia side effects.

3.2. Baseline Procedures:

Before the study patients will have a physical examination and medical history will be obtained. We will ask the following questions:

1. Have you had back pain lasting longer than one week during pregnancy?
2. Did you have back pain for more than 3 months prior this pregnancy?
3. Have you taken pain medications for pain for more than 3 months?

Routine intrapartum and postpartum care will be provided by the subjects' clinical providers. Trained and experienced research staff will be responsible for all research data abstraction. The PI and collaborators will review and validate the outcomes for all subjects identified to have the primary outcomes. If there is uncertainty, a second PI will review the chart, discuss with the other PI's as needed, and make a final determination regarding the outcome.

Outcomes and variables will be assessed in the hospital at VISIT#1 and VISIT#2.

3.3. Follow-up: No follow up visits will be needed for this study. The subject participation will be considered complete when the subject is discharged from the hospital (either 24hrs or 48hrs postpartum).

3.6. Withdrawals: Subjects who withdraw from the study after inclusion will be excluded from further follow-up. Data collected until the time of withdrawal will be analyzed.

3.7 Outcomes

Primary outcome: Successful epidural catheter placement on the first needle insertion attempt. An epidural insertion attempt will be defined as advancement of the needle in an effort to enter the epidural space; a needle requiring withdrawal for redirection or reinsertion through the skin/another skin puncture will be counted as an additional attempt. Staff intervention occurred if the trainee required more than six attempts. A failed technique will be defined as an epidural catheter requiring replacement during labor or general anesthesia for cesarean delivery after inadequate analgesia from epidural analgesia. Early and late failures were defined according to whether the catheter required replacement within or after the first 90 min following insertion, respectively.

Secondary outcomes: numbers of needle redirection, skin passages by needle, and puncture sites, and rates of spinal headache, spinal/epidural hematoma, epidural/spinal abscess, and conversion general endotracheal anesthesia. Procedure duration starting from screening with ultrasound to the end of the epidural catheter taped. Twenty-four hours post-partum, parturient satisfaction with analgesia during labor was assessed using the Numerical Rating Scale (NRS). Procedural difficulty will be rated by the performing anesthesiologist on a 10-point Likert scale from one (easy) to ten (extremely difficult).

We will also record thouy needle depth from skin and measured depth by ultrasound.

4. Criteria for inclusion of subjects:

- American Society of Anesthesiologists physical status class I, II, or III.
- Age between 18 and 50.
- Term pregnancy.
- Requesting epidural analgesia for anticipated vaginal delivery.
- BMI>or = 37.

5. Criteria for exclusion of subjects:

- Contraindication for epidural analgesia (bleeding diathesis, neuropathy, severe scoliosis, previous spine surgery, local anesthetic allergy).
- Inability to adequately understand the consent form.
- Incarcerated patients.
- Patients with known spinal deformities.
- Allergies to ultrasound gel.
- Allergies to local anesthetics (lidocaine, bupivacaine and etc)

6. Sources of research material: Electronic medical records.

7. Recruitment Methods and Consenting Process: See 3.1 above.

8. Potential Risks

8.1. Randomization risk

The subject will receive the standard of care regardless of group allocation. If randomized to the active treatment, they may have risk of adverse response to the antibiotic.

8.2. Loss of Confidentiality

Anytime information is collected, there is a potential risk for loss of confidentiality. Every effort will be made to keep subject's information confidential; however, this cannot be guaranteed.

8.3. Adverse Effects and Risks

This is non-invasive 3D ultrasound device so there are no potential risks to mother or baby by using this 3D ultrasound device. Risks and complications for epidural catheter placement are same either patients on study or not.

Reaction to ultrasound gel: There is a minor risk of a skin reaction to the ultrasound gel, which is unlikely. If it does occur, treatment will be given.

Algometer measurements: The potential discomfort associated with pressure sensitivity measurements is bruising and/or tenderness of the region tested. The investigators tested the pressure sensitivity testing on themselves and found the discomfort to be mild if pressure was limited to 60 Newtons force. The pressure will be limited to 60 Newtons force.

Epidural catheter placement: The risks of epidural are unchanged from those of standards of care. The major risks are bleeding, infection, nerve damage (1 in 100-300,000), reaction to medications, failure to relieve pain (~5%), dural puncture, headache due to the dural puncture (~1%), epidural hematoma (1 in 100-300,000), paralysis (1 in 100-300,000), transient nerve injury (1 in 2-6,000), seizure (1 in 10,000 or more), and cardiac or respiratory arrest (Extraordinarily rare. 1 in many hundreds of thousands). The major risks are unlikely but if they occur they will require additional testing and treatment. The minor risks are difficulty moving legs (10%) (During the epidural and a few hours after delivery) nausea, vomiting, itching (20-60%), urinary retention, and hypotension (mild: 10-20%; severe: 1 in 1000). These risks are more common and easily treatable.

9. Subject Safety and Data Monitoring

The PI and research collaborators will be responsible for monitoring the safety of this study. The report will include participant demographics, expected versus actual recruitment rates, summary of any quality assurance or regulatory issues, summary of adverse events (AEs) or serious adverse events (SAEs) which may have occurred, and any changes in the protocol as a result of these issues.

The PIs and collaborators will ensure all aspects of **data quality** including monitoring for adherence to consent procedures, inclusion and exclusion criteria, valid abstraction, correct entry, timeliness and responsiveness to data queries.

Data will be collected and stored with the participant ID code only. The master enrollment log linking subject identifiers with study ID numbers will be kept in a

password-protected database on the Obstetrics and Gynecology Department's internal server separate from the data. Several data collection forms will be used. Data on these forms devoid of personal identifiers will be securely stored at our perinatal research division. The research coordinator will be available to monitor the data and correct any discrepancies based on source documents if needed.

10. Potential Benefits:

We hope that this novel approach will be beneficial in assessing the optimal space for epidural analgesia in morbid obese parturient, leading to better patient satisfaction, better pain control, faster procedure times and less adverse effects.

11. Procedures to Maintain Confidentiality:

- The data collected will be indirectly linked to the subject by subject's MRN number.
- When the subject agrees to participate in the study, a subject number will be assigned to the subject - from 1 to 308 - and this number will be entered on the data collection sheet.
- The data collected will be transferred to the PI's password-secured UTMB computer that is stored in a locked room using a USB flash drive.
- The study PI will be the only person to have a list with the number designated to each subject and the corresponding subject's MRN number. This list will be kept in a locked cabinet of the PI's locked UTMB office. This identifier is needed to access and analyze demographic data. During analysis of the data, all identifiers will be deleted.
- Data will not be disclosed to outside persons or entities.

12. **Statistical approach:** Analysis will be performed by intent to treat. Univariate analysis will be used to describe the population in the study. For this analysis normality will be tested using Shapiro-Wilk method. Demographics will be analyzed by descriptive

statistical methods such as Student t, Mann-Whitney, Pearson's chi square, or Fisher Exact tests as appropriate. Continuous data will be reported as median +/- IQR or mean +/- SDEV. Statistical analyses of primary and secondary outcomes between two groups will be performed by chi-square or Fisher Exact test as appropriate. Relative risk and 95% confidence intervals will be calculated.

Sample size was calculated using a superiority trial design. The primary outcome will be the occurrence of more than one needle insertion, which will be compared between the two study groups. From the available data from prior studies of 50-70% incidence of more than one needle insertion rates in the obese population and estimating treatment effect to be 33% with 80% power and alpha of 0.05: The total estimated sample size is 280. Assuming 10% loss to follow, this study proposes a total of 308 subjects will be needed to complete the study. The STATA 14 (Dallas, TX) will be used for statistical computations. This trial will be registered with Clinicaltrials.gov before recruitment is initiated and after IRB approval.

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