Protocol Title:

Evaluation of the Compuflo Epidural Instrument for Thoracic Epidural Space Identification

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Objectives:

Purpose of this pilot study is to evaluate whether this injection pump technology, which is FDA approved for lumbar epidural anesthesia, is also capable of identifying the thoracic epidural space through measurement of pressure levels. While this device is approved by the FDA for use in the procedure of the lumbar epidural, it is not actually used to perform the epidural procedure but rather to measure the epidural pressure. This study will likewise measure the epidural pressure.

Background:

A successful and safe performance of epidural anesthesia/analgesia in the perioperative setting relies on correct identification of the epidural space (ES) by the operator. Multiple methods for objective and more or less simple identification of the ES have been proposed such as waveform analysis (1), nerve stimulation (2), fiber optical or ultrasound guidance (3,4), and acoustic signal assistance (5).

However, none of these suggested techniques is currently standard of care and most anesthesiologists and/or pain physicians still utilize the subjective manual feeling of a loss of resistance (LOR).

Consequently, reported epidural failure rates using LOR for ES identification vary greatly and can range for instance for labor epidural analgesia from 1.5% up to 23%, if a standardized definition of epidural failure is applied (6,7). Failure rates for epidural analgesia for postoperative pain management after major surgery are even higher and can reach up to 27% for lumbar and 32% for thoracic epidurals (8).

Previously, the now FDA approved Compuflo Epidural Instrument has been demonstrated to successfully and safely identify the lumbar epidural space. This technology allows for real-time pressure readings at the epidural needle tip, which are displayed in digital and graphical fashion.

This study is designed to evaluate this technology for ES identification when performing thoracic epidural anesthesia.

1) Leurcharusmee P, Arnuntasupakul V, Chora De La Garza D, Vijitpavan A, Ah-Kye S, Saelao A, Tiyaprasertkul W, Finlayson RJ, Tran DQ. Reliability of Waveform Analysis as an Adjunct to Loss of Resistance for Thoracic Epidural Blocks. Reg Anesth Pain Med. 2015; 40: 694-7

2) Tsui BC, Gupta S, Finucane B. Confirmation of epidural catheter placement using nerve stimulation. Can J Anaesth. 1998; 45: 640-4

3) Kuo WC, Kao MC, Chang KY, Teng WN, Tsou MY, Chang Y, Ting CK. Fiber-needle swept-source optical coherence tomography system for the identification of the epidural space in piglets. Anesthesiology. 2015; 122: 585-94

4) Vallejo MC, Phelps AL, Singh S, Orebaugh SL, Sah N. Ultrasound decreases the failed labor epidural rate in resident trainees. Int J Obstet Anesth. 2010;19: 373-8

5) Lechner TJ, van Wijk MG, Maas AJ. Clinical results with a new acoustic device to identify the epidural space. Anaesthesia. 2002; 57: 768-72

6) Crawford JS. The second thousand epidural blocks in an obstetric hospital practice. Br J Anaesth 1972; 44: 1277-1286

7) Thangamuthu A, Russell IF, Purva M. Epidural failure rate using a standardised

definition. Int J Obstet Anesth. 2013; 22: 310-5
8) Ready LB. Acute Pain: lessons learned from 25,000 patients. Reg Anesth Pain Med 1999; 24: 499-505

Inclusion criteria:

Patients aged between 18 and 80 years inclusive. Body mass index (BMI) between 18.5 and 40 inclusive. Patients scheduled to undergo thoracic epidural anesthesia as part of the planned anesthetic management.

Exclusion criteria:

Patients younger than 18 years of age or older than 80 years of age. Patients with a BMI less than 18.5 or greater than 40. Patients with contraindications for thoracic epidural anesthesia. Patients with an allergy to local anesthetics. Patients with preexisting nerve damage. Patients who are unable to provide informed consent. Individuals who are not yet adults, pregnant women, and prisoners will not be included.

Procedures Involved:

After IRB approval and patient informed consent, a total of 20 patients scheduled to receive thoracic epidural needle placement, as part of their scheduled medical management, will be enrolled in this prospective observational trial (NTC…) at the University of Miami Hospital and Jackson Memorial Hospital

The study will be conducted in 2 phases. In Phase A, 10 patients will have their ES identified with the traditional LOR technique and the Compuflo Epidural Instrument will be solely used to obtain pressure readings once the ES has been reached. In Phase B 10 patients will have their ES identified with the Compuflo epidural Instrument and the LOR technique will be used for confirmation.

<u>Phase A – Thoracic Epidural Space Identification with traditional LOR:</u>

Patients will receive thoracic epidural anesthesia in the following fashion:

After attaching American Society of Anesthesiologists standard monitors, patients will be placed in a sitting position. Following disinfection and preparation in the usual fashion, an epidural Tuohy needle will be introduced at a thoracic level o to a depth of approximately 3cm. The epidural Tuohy needle will then be connected to a 3-way stopcock with a loss of resistance syringe filled with normal saline connected to the in-line port and the Compuflo Epidural Instrument connected to the side-port. The stopcock will be turned “Open” to the LOR syringe and “Close” to the Compuflo Epidural Instrument. The operator will then advance the epidural Tuohy needle until a loss of resistance is perceived. The stopcock will then be turned “Open” to the Compuflo Epidural Instrument and “Close” to the LOR syringe. The Compuflo Epidural Instrument will be started at an infusion rate of 0.050ml/sec of normal

saline for 30 seconds. The pressure readings will be graphically and digitally recorded.

The Compuflo Epidural Instrument will then be stopped and the stopcock will be disconnected from the Tuohy needle. After disconnection of the epidural Tuohy needle, an epidural catheter will be advanced at the discretion of the operator. After removal of the epidural needle and securing of the epidural catheter, a 3 mL epidural test dose consisting of lidocaine (15 mg/mL) with epinephrine (5 mcg/mL) will be given to rule out intrathecal or intravascular catheter position. Epidural anesthesia will then be established at the discretion of the operator by dosing the epidural catheter with a local anesthetic of their choice and a volume of their choice. Fifteen to thirty minutes after dosing the epidural catheter a blinded investigator will assess the patient for sensory and motor blockade. Successful performance of epidural anesthesia will be defined as a loss of sensation to cold in at least one dermatome, either unilateral or bilateral. If an epidural catheter cannot be advanced into the epidural space, the epidural Tuohy needle will be withdrawn to a depth of 3cm or completely removed and inserted at a new puncture site and a new attempt of epidural Tuohy needle insertion and identification of the epidural space with the loss of resistance technique will begin. After a maximum of 3 failed attempts, epidural space identification will be considered unsuccessful

<u>Phase B – Thoracic Epidural Space Identification with the Compuflo Epidural Instrument:</u>

Patients will receive thoracic epidural anesthesia in the following fashion:

After attaching American Society of Anesthesiologists standard monitors, patients will be placed in a sitting position. Following disinfection and preparation in the usual fashion, an epidural Tuohy needle will be introduced at a thoracic level o to a depth of approximately 3cm. The epidural Tuohy needle will then be connected to a 3-way stopcock with a loss of resistance syringe filled with normal saline connected to the in-line port and the Compuflo Epidural Instrument connected to the side-port. The stopcock will be turned "Close" to the LOR syringe and "Open" to the Compuflo Epidural Instrument. The Compuflo Epidural Instrument is started and set to infuse normal saline at a rate of 0.050ml/sec with a pressure limit of 100mmHg. The operator will then slowly advance the epidural Tuohy needle until the Compuflo Epidural Instrument indicates that the ES has been reached. This is achieved by observation of a drop of pressure of at least 50mmHg sustained for at least 5 seconds ("low pressure plateau"). The Compuflo Epidural Instrument will then be stopped and the stopcock will be turned "Close" to the Compuflo Epidural Instrument and "Open" to the LOR syringe. Once the operator has confirmed correct ES identification with the LOR syringe, the stopcock will be disconnected from the Tuohy needle.

After disconnection of the epidural Tuohy needle, an epidural catheter will be advanced at the discretion of the operator. After removal of the epidural needle and securing of the epidural catheter, a 3 mL epidural test dose consisting of lidocaine (15 mg/mL) with epinephrine (5 mcg/mL) will be given to rule-out intrathecal or intravascular catheter position. Epidural anesthesia will then be established at the discretion of the operator by dosing the epidural catheter with a local anesthetic of their choice and a volume of their choice. Fifteen to thirty minutes after dosing the

epidural catheter a blinded investigator will assess the patient for sensory and motor blockade. Successful performance of epidural anesthesia will be defined as a loss of sensation to cold in at least one dermatome, either unilateral or bilateral. If an epidural catheter cannot be advanced into the epidural space, the epidural Tuohy needle will be withdrawn to a depth of 3cm or completely removed and inserted at a new puncture site and a new attempt of epidural Tuohy needle insertion and identification of the epidural space with the loss of resistance technique will begin. After a maximum of 3 failed attempts, epidural space identification will be considered unsuccessful.

Follow up:

Patients will be evaluated in a timeframe of 12h-24h after epidural catheter removal for potential complications. A sensory and motor exam will be performed. Patients will also be evaluated for any symptom of post-spinal-puncture headache. Patients who did not receive epidural anesthesia due to inability to identify the epidural space will be evaluated in the same fashion in a timeframe of 12-24h after attempted epidural anesthesia.

Data collection:

Data will be collected on case report forms. Demographic data of each patient (weight, height, age, gender) will be recorded at the beginning of each case.

Pressure readings from the Compuflo Epidural Instrument will be recorded once the epidural space is reached in Phase 1 of the study, and throughout the procedure in Phase 2. Success rate of epidural anesthesia and complications will be recorded.

Data will be stored in individual study folders and locked in a Division of Regional Anesthesia faculty office.

Data management

Demographical data and pressure readings will be analyzed by calculating a mean and standard deviation. Success rates and incidence of complications will be recorded in percentages and a median including 25^{th} to 75^{th} percentile range will be calculated.

Risks/ Benefits

In Phase 1 of the study, there will be no personal direct benefit and minimal risk for harm since the Compuflo Epidural Instrument will be solely used for the purpose of measuring pressures while the actual performance of thoracic epidural anesthesia will be with the traditional LOR method.

In Phase 2 of the study, the patient may directly benefit from the more objective identification method of the epidural space with the Compuflo Epidural Instrument. A potential risk is electrical failure of the computerized injection pump; in such case, the operator will revert back to the traditional LOR technique.

Setting:

Research consents will be obtained in the operating room holding area of the University of Miami Hospital or Jackson Memorial Hospital, as applicable, for patients admitted the day of the procedure. In hospital patients will be consented

the night prior to the procedure in their admitted locations. This study will take place at University of Miami Hospital or Jackson Memorial Hospital.

Resources available:

Dr. Ralf E. Gebhard is a Professor of Clinical Anesthesiology and Director of the Division of Acute Pain Medicine and Regional Anesthesia in the Department of Anesthesiology, Perioperative Medicine and Pain Management at the University of Miami Miller School of Medicine. He has conducted substantial previous research as the principal investigator in multiple clinical trials in the area of acute pain and regional anesthesia. Dr. Gebhard will be responsible for overseeing the recruitment, consent, collection and storage of data as well as performing the measurements described in the procedure section.

Dr. Robyn Weisman is an Assistant Professor in Clinical Anesthesiology and in the Division of Acute Pain Medicine and Regional Anesthesia. She has participated in investigator-initiated research and authored manuscripts in anesthesiology previously and is well versed in research compliance.

The study coordinators are experienced in conducting clinical research for clinical trials and investigator-initiated studies. They will assist the investigators in study-related activities.

Patient Recruitment Methods:

Potential subjects will be identified by the study team based on the scheduled procedures to be done by the Regional Anesthesia team. Patients on the schedule will be pre-screened using available medical data for exclusion criteria. If patients do not meet any of

the exclusion criteria they will be visited by the Principal Investigator, Sub-investigator and/or Study coordinators on the morning of surgery or the night before depending on their admission status. If the subject is currently an inpatient at the hospital, the medical team taking care of the patient will be approached by the study team to get permission to approach the subject. Study details, risks, benefits and alternatives will be discussed with each potential subject. If the patient shows interest into the study, the PI will notify research personnel of potential participant to start the process of consent. Study information and informed consent document (attached) will be provided to each subject. If the patient agrees to the study a copy of the signed consent will be provided to the patient and one placed in the patient medical chart. The original document will be placed in the study specific subject folder.

Local number of subjects:

A total of 20 patients will be expected to be enrolled into this pilot study.

Confidentiality:

Data will be recorded on study sheets locked in a Division of Regional Anesthesia faculty office in a locked filing cabinet for the period of one year. Additionally, data will be stored on a password protected University of Miami computer in the Department of Anesthesiology in Suite 3075, 1400 NW 12th Avenue, Miami, Florida, 33136. Only study personnel listed on the IRB protocol will have access to the data. All study records and documents, will be retaind for studies that are subject to both

FDA and HIPAA regulations: According to HIPAA regulations will be retained for a minimum of six years following study closure. Our research department will retain all research data until the later of these dates. The data will be destroyed after this time in accordance with university policies.

Consent process:

Written informed consent will be obtained for each subject in English-speaking subjects only. Subjects who do not speak English will not be enrolled. Research consent will be obtained in the operating room holding area of University of Miami Hospital for patients admitted the day of the procedure. In hospital patients will be consented the night prior to the procedure in their admitted locations.

Patient's identity and age will be verified prior to obtaining informed consent, as well as their understanding of risks and benefits and possible alternatives available explained before any informed consent signature from those patients willing to participate. The PI(s) with each study participant will:

• Ensure each patient is given full and adequate oral and written information about the nature, purpose, possible risk, and benefit of the study.

• Ensure each patient is notified that they are free to discontinue from the study at any time.

• Ensure that each patient is given the opportunity to ask questions and allowed time to consider the information provided.

• Ensure each patient provides signed and dated ICF before conducting any

procedure specifically for the study.

• Ensure the original, signed ICF(s) is/are stored in the investigator's Study File.

• Ensure a copy of the signed and dated ICF is given to the patient for future reference of the study.

• Ensure that any incentives for patients who participate in the study as well as any provisions for patients harmed as a consequence of study participation are described in the ICF that is approved by an IEC/IRB.

All potential subjects will be given ample time to review the consent form and discuss any questions and concerns with research personnel or study doctor, and will be provided with a copy of the signed ICF. Consent will be documented with a dated signature on the consent form from both the patient and the study personnel conducting the consent discussion.