HOSPITAL FOR SPECIAL SURGERY

electronic Clinical Application Portal (eCAP)

Date: Friday, August 18, 2017 12:27:29 PM
ID: 2017-1304

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Study Identification Information

This is the first step in your Human Research Application. You will automatically be guided to the appropriate forms needed to complete your submission.

1.0 Title: (please do not use initials)
The effect of dexmedetomidine dose on motor evoked potentials during spine surgery: A randomized, single-blind trial

* **Short Title for EPIC:**
Dexmedetomidine and MEPs during spine surgery (If Not Applicable, please enter N/A)

2.0 Description:
This parallel group, two-arm, randomized superiority trial will compare the effect of two different doses of dexmedetomidine on motor evoked potentials during spine surgery.

3.0 * Principal Investigator:
Ronald Emerson, MD

4.0 Study Contact:

5.0 Co-Investigators:

First Name	Last Name	Organization
Matthew	Cunningham, MD, PhD	Spine
Kara	Fields	Research
Han Jo	Kim, M.D.	Spine
Frank	Schwab, M.D.	Spine
Michael	Urban, MD PhD	Anesthesiology

If a name does not appear in Co-Investigators directory, please contact zhouy@hss.edu to have an eCAP account created.

6.0 Other Study Staff/Collaborators:

FirstName	LastName	Organization	Email	Role
There are no items to display				

7.0 * Type of Application:

- (●) **Clinical Research Proposal**
- ( ) Expedited Retrospective Chart Review
- ( ) Request for Exemption
- ( ) New Registry
- ( ) Existing Approved Registry

Please click *here* to preview Exempt Categories.

Click *here* to preview Study Designs.

8.0 Select appropriate funding sources for this study:

Name
Internally Funded Support

Other Funding Sources:

Note: If the funding source of the study is 'Industry Funded Support', Clinical Research Administration (CRA) will be notified.

If your study requires CRA review, please upload applicable documents, including sponsor protocol, drug brochure, etc :

Name	Version
There are no items to display	

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CRP Information

1.0 The proposal should be submitted to the appropriate Clinical Review Panel (CRP) for scientific review. If you are unsure of which Clinical Review Panel to select, please contact Barbara Bosco at 212.606.1914

*

Name
Neurology

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Regulatory Status of Drugs and Devices

1.0 The regulatory status of the drugs or devices in this research proposal is:

Name
Approved for use by the FDA and being used according to “label” (for approved indication)

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FDA Approved Drugs/Devices

1.0 Add all FDA Approved Drugs administered in this study:

Drug Name	Manufacturer	Drug Name (if other)	Manufacturer (if other)
Other		Dexmedetomidine	Pfizer
		Propofol	Pfizer

2.0 Add all FDA Approved Devices administered in this study:

Device Name	Manufacturer	Device Name (if other)	Manufacturer (if other)
View		Cadwell Cascade	Cadwell, Inc.
View		NICOM	Cheetah Medical

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Pharmacy Involvement / Impact to EPIC

1.0

Is this an inpatient study?

(●) **Yes** ( ) No

2.0 * Will this study have Investigational Drug Service involvement? (Pharmacy will be purchasing/dispensing any medications being used and/or study requires placebo and patient randomization)

( ) Yes (●) **No**

3.0

If the answer to either question is yes, please explain briefly below AND contact Mylinh Duong at 646.797.8410 (duongm@hss.edu) or Nicole Oliva at 646.797.8324 (OlivaN@hss.edu).

This is an inpatient study to be performed during surgery. Anesthetic drugs to be

used are routinely used during surgery and will not require pharmacy involvement.

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Study Locations

1.0 Select the Research Facilities where this study will be conducted:

Facility

HSS

1.1 If Other, please specify:

2.0 * Is this a multi-Center study?

No

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This section will be reviewed by the appropriate Clinical Review Panel. Each of the headings in this section must be addressed.

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Specific Aims or Research Questions

1.0 What is the condition or intervention to be studied?

Please click Here for example.

We will study motor evoked potentials under two anesthetic conditions, one using propofol and lower dose of dexmedetomidine, another using a lower dose of propofol with a higher dose of dexmedetomine during multilevel posterior spinal fusions.

2.0 What is/are the research question(s)/specific aim(s)? Pose very specific questions that can be addressed within the proposed design of the study. Prioritize them in order of

importance.

Aim 1 (definitive): To compare the percentage of spine cases with monitorable motor evoked potentials (MEPs) for the purpose of monitoring spinal cord integrity under two anesthetic conditions, one using a higher dose of propofol and a lower dose of dexmedetomidine, and the other using a lower dose of propofol and a higher dose of dexmedetomidine.

Aim 2 (exploratory): To estimate the difference in percentage of spine cases with monitorable MEPs for the purpose of monitoring nerve root integrity between two anesthetic conditions.

Aim 3 (exploratory): To estimate the association between MEP metrics (peak to peak amplitude, waveform integral, waveform line-length, trial variability of peak to peak amplitude, trial variability of waveform integral, and trial variability of waveform line-length) and cardiac output.

3.0 What is/are the hypothesis(es)?

There will be a difference in the percentage of spine cases with monitorable MEPs for the purpose of monitoring spinal cord integrity under two anesthetic conditions.

4.0 Identify and define the primary outcome and when the outcome will be measured. If measuring change in post-operative function is the most important, that will be your primary outcome.

Monitorable MEPs for the purpose of monitoring spinal cord integrity (yes vs. no). This outcome measure will be assessed during the initial two hours of surgery following induction of anesthesia and establishment of stable anesthesia. MEP recordings will be obtained in sets of 3-4 trials, approximately every 15-20 minutes, as permitted by the surgeon.

Monitorable will be defined as having MEPs present in 3 muscles in each lower extremity, with mean peak-to-peak amplitude of at least 50 uV, with mean-normalized interquartile variability of 0.9 or less.

5.0 Identify and define the secondary outcome(s) and when they will be measured (list additional goals one at a time with their corresponding outcomes).

1) Monitorable MEPs for the purpose of monitoring nerve root integrity present at all assessments (yes vs. no). For this purpose, MEPs will be separately assessed in quadriceps, tibialis anterior, extensor hallucis longus, medial gastrocnemius and abductor hallucis in each lower extremity. Monitorable will be defined as having MEPs with mean peak-to-peak amplitude of at least 50 uV, with mean-normalized interquartile variability of 0.9, separately for each muscle. This outcome measure will be made during the first two hours of surgery following induction of anesthesia

and establishment of stable anesthesia.

2) MEPs (peak to peak amplitude, waveform integral, waveform line-length, trial variability of peak to peak amplitude, trial variability of waveform integral, and trial variability of waveform line-length) measured in quadriceps, tibialis anterior, extensor hallucis longus, gastrocnemius, and abductor hallucis. These measures will be calculated from data recorded throughout the case, following establishment of stable anesthesia through the conclusion of surgery.

3) Cardiac output, measured continually during surgery.

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BACKGROUND - Be sure to answer each question individually

1.0 Explain why these research questions are being asked:

Many general anesthetic agents can affect MEPs in ways that can make them difficult to monitor and can confound their interpretation. Dexmedetomidine in increasingly being used as a component of total intravenous anesthesia during surgery requiring MEP monitoring. It is therefore important to determine the effect of dexmedetomidine of MEPs.

Optimal fluid management is challenging during complex spine surgery accompanied by large amounts of blood loss, for reasons detailed in 2.0. This study aims to determine if there a correlation between MEP waveform measures and cardiac output, that could potentially could be useful as a guide to fluid management.

Peak-to-peak amplitude is the most commonly clinically employed measure of MEPs. For reasons discussed in 2.0, the integral of the rectified waveform or waveform line-length may be superior measures.

2.0 What is the background of the topic that you believe is important for the reviewer to know in considering this protocol, including prior studies by this research team. Describe strengths and deficiencies of prior studies; explain how this study fits in. Include references.

Motor evoked potentials (MEP), monitored during spine surgery as measures of spinal cord integrity, are known to be attenuated in a dose related fashion by nitrous oxide and volatile anesthetic agents. Propofol has been shown to better preserve MEPs. For this reason, propofol is commonly used, along

with an opioid and often ketamine, for cases requiring MEP monitoring. The addition of dexmedetomidine to total intravenous anesthesia during spine surgery has recently been shown to reduce the required propofol dose as well as improve the quality of recovery, possibly related to decrease the release of cytokines. Reduction of propofol dose is desirable, both because of rare metabolic risks as well as the known effect of delayed emergence [1-8].

A challenge for the anesthesiologists during complex spine surgery is to maintain end organ perfusion despite large blood losses in an attempt to prevent devastating complications such as spinal cord ischemia, ischemic optic neuropathy (ION), renal failure, myocardial ischemia and stroke. The best approach to achieve euvolemia and prevent end-organ ischemia and metabolic acidosis is still a dilemma. Despite the ubiquitous use of central venous pressure (CVP) monitoring during large blood loss procedures, there is a poor direct correlation between CVP and blood volume, as well as the ability of changes in CVP to predict the hemodynamic response to a fluid challenge. Volume resuscitation with a pulmonary artery catheter (PAC) has been shown to be beneficial during adult reconstructive spinal surgery. However, multiple published reports have questioned the value of PAC monitoring. Arterial and central venous blood gas analysis may provide information regarding tissue oxygenation requirements and perfusion. Urine output alone correlates poorly with adequate tissue perfusion, since oliguria may be a consequence of excess antidiuretic hormone release rather than hypovolemia and therefore, attempts to increase urine output intraoperatively may result in excessive fluid administration. Devices which measure arterial pulse pressure variation and provide non-invasive cardiac output measurements have been shown to be efficacious in providing goal directed fluid therapy during complex spine procedures. The Cheetah NICOM uses thoracic bioreactance, a measure based on phase modulation of an oscillating current traversing the thoracic cavity, to noninvasively measure cardiac output and fluid responsiveness. Cardiac output measured by the NICOM device has been shown to correlate with measurements made by thermodilution and pulse contour analysis, and has been found to be efficacious in fluid management during large blood loss procedures [9-12].

Motor evoked potentials are dependent on adequate perfusion in watershed regions along anterior spinal artery, as well as within the gray matter of the lumbar enlargement. As such, they are highly sensitive to hemodynamic effects [13]. Anecdotal observations suggest that MEP changes, particularly changes observed in MEPs from higher stimulation threshold muscles, may be early indictors of inadequate perfusion. This study aims to better characterize this relationship, and determine whether MEP changes precede changes in measured cardiac output, potentially serving as guides to fluid management.

The motor evoked potential signal is a complex polyphasic waveform comprising the sum of signals generated by individual motor units within the listening spheres of the recording electrodes; approximately 5% of motor units in a large muscle are sampled in the typical clinical recording. Ideally, a MEP metric would be linearly proportional to the number of motor units activated. Although most commonly employed clinically, it is unlikely that peak-to-peak amplitude is ideal, because the signals from individual motor units are asynchronous with varying phase relationships, and are influenced

unevenly by proximity the recording electrodes. The extreme case, occasionally encountered, is a large, brief, biphasic signal, with large peak-to-peak amplitude, probably generated by a single motor unit very close a recording electrode [13]. Although also imperfect, it is likely that the integral of the rectified waveform, or line-length of the waveform, may well be better measures. The strength of correlation of each of these measures to cardiac output may inform selection of the most robust measure.

MEP signals commonly exhibit considerably trial-to-trial variability. This variability does not reflect “measurement error”, but rather reflects spontaneous fluctuation of motor-pool excitability resulting in changing motor unit contributions to the MEP signal. Trial-to-trial variability is influence by numerous factors, including anesthesia and hemodynamics. If shown to correlate with cardia output, MEP (peak-to-peak amplitude, integral, line-length) variability, may also provide additional, useful, metrics.

1. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: A novel sedative-analgesic agent. Proc (Bayl Univ Med Cent) 2001;14:13–21.

2. Liolios A, Guerit JM, Scholtes JL et al. Propofol infusion syndrome associated with short-terms large dose infusions during surgical anesthesia in an adult. Anesth Analg 2005;100:1804-6.

3. Grottke O, Dietrich PJ, Wiegles S et al. Intraoperative wake-up test and postoperative emergence in patients undergoing spinal surgery: A comparison of intravenous and inhaled anesthetic technique using short acting anesthetics. Anesth Analg 2004;99:1521-1527.

4. Dutta S, Karol MD, Cohen T, et al. Effect of dexmedetomidine on propofol requirements in healthy subjects. J Pharm Sci. 2001; 90:172-81.

5. Mahmoud M, Sadhasivam S, Sestokas AK,et al. Loss of transcranial electric motor evoked potentials during pediatric spine surgery with dexmedetomidine. Anesthesiology. 2007;106:393-6

6. Bala E, Sessler DI, Nair DR et al. Motor and somatosensory evoked potentially are well maintained in patients given dexmedetomidine during spine surgery. Anesthsiology 2008; 109:417-425.

7. Tobias JD, Gobel TJ, Bates G, et al. Effects of dexmedetomidine on intraoperative motor and somatosensory evoked potential monitoring during spinal surgery in adolescents. Ped Athesth 2008; 18: 1082-1088.

8. Li Y, Meng L, Peng Y, et al. Effects of dexmedetomidine on motor- and somatosensory-evoked potentials is patients with thoracic spinal cord tumor: a randomized controlled trial. BMC Anesthesiol 2016:16;51.

9. Kossari N, Hufnagel G, Squara. Bioreactance: A new tool for cardiac output and thoracic fluid content monitoring during hemodialysis. Hemodialysis International. 2009;13:512-517.

10. Marik P et al. The use of bioreactance and carotid Doppler to determine volume responsiveness and blood flow redistribution following passive leg raising in hemodynamically unstable patients. Chest 2013; 143:364-370.

11. Waldron N et al. A prospective comparison of a noninvasive cardiac output monitor versus esophageal Doppler monitor for goal directed fluid therapy in colorectal surgery patients. Anesth Analg 2014; 118:966-75.

12. Dunham, CM et al. Emergency department noninvasive (NICOM) cardiac outputs are associated with trauma activation, patient injury severity and host conditions and mortality. J Trauma Acute Care Surg. 2012; 73:479-85.

13. MacDonald DB, Skinner S, Shills J and Yingling C. Motor evoked potential monitoring - a position statement of the American Society for Neurophysiological Monitoring. Clinical Neurophsiology 2013;124:2291-2316.

3.0 Identify specific gaps in current knowledge that this study is intended to fill.

Both propofol and dexmeditomidine produce dose-related attenuation of MEPs. There is limited data concerning the combined effect of the two agents. Taken together, the limited available literature suggests that combined with propofol at 70 ug/kg/min, dexmeditomidine 0.5 ug/ml/hr does not produce significant attenuation of MEPs, although attenuation of MEPs may occur when it is combined with higher propofol doses. Significant attenuation of MEPs is more frequent at higher doses of dexmedtomidine in combination with propofol, although previous studies have been conducted using propofol doses higher than are proposed in this study.

It is not known whether MEP changes may be useful as guides for fluid management during complex spine procedures.

The optimal metric for quantitative characterization of MEPs in not known.

4.0 How will answering these questions change clinical practice, change concepts about the topic or confirm the work of other investigators?

This study will inform the best practice of intraoperative monitoring by establishing acceptable doses of dexmeditomidine, in combination with propofol, for use in conjunction with MEP monitoring. This study will also provide insight into the relationship between MEPs and cardiac output, and provide insight into whether MEP changes may potentially be useful into the management of fluid status during spine surgery. This study will also provide insight into improved MEP metrics, that, perhaps in the future, could be incorporated into clinical recording systems.

5.0 Is this a pilot study that could lead to a more definitive protocol or different study? (●) **Yes** ( ) No

5.1 If you answered No, please explain below:

6.0 Please upload reference or additional document here (if needed).

Name	Description
There are no items to display	

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Study Design

1.0 Observational:

Name	Description
There are no items to display	

2.0 Experimental:

Name	Description
Randomized Controlled Clinical Trial	This is the “gold standard” for clinical research. These prospective studies have at least two groups. Patients meeting strict inclusion/exclusion criteria are enrolled and randomly assigned to receive either an experimental intervention or to receive what is considered to be an acceptable alternative – usually the current standard of care or a placebo (e.g., study of hylauronic acid injection versus cortisone for arthritis).

2.1 If Other, please specify:

2.2 If Randomized Controlled Clinical Trial is selected, please choose one of the following:

Name
Other

If other, please list name or indicate N/A below:

Randomized trial of different doses of standard FDA approved anesthetics.

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Recruitment

1.0 Check all that apply to describe your study population:

Population

Patients

Vulnerable Populations
There are no items to display

1.1 If Other, please specify:

2.0 Inclusion Criteria: *list characteristics that potential subjects and controls need to have. Use a bullet format, if applicable*.

- Subjects will be within the age range of 18 – 70 years.
- Subjects will be patients undergoing multi-level posterior spine fusions requiring MEP monitoring

3.0 Exclusion Criteria: *list characteristics that would cause you to exclude potential subjects and controls.*

Justify any age, ethnicity, language, or gender-based exclusion criteria. *Use a bullet format, if applicable*.

- Allergy to any of the anesthetic medications included in the protocol
- Non-English speaking
- Younger than 18 and older than 70 years of age
- Any other surgery other than multi-level posterior spine fusions

4.0 Age Range:

18-70 years

5.0 Describe how you will identify and recruit potential subjects for participation in the study.

Potential patients will be recruited as a consecutive series of patients undergoing multi-level posterior spine fusions requiring MEP monitoring. Recruitment will begin following approval of the study, and will be conducted by the principal investigator or an IRB approved co-investigator.

6.0 * **Please select enrollment type from following drop down list:**
Over Course of Study

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Target Enrollment

1.0 * **What is the maximum number of subject you plan to enroll in this study at HSS?(Please enter a number)**
68

2.0 **If this is a multi-center study, indicate the projected total subject accrual across all sites.**

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Patients

1.0 **Please check the box(es) below that best reflect how patients will be identifed and recruited for participation.**

	How subjects will be identified
☑	**Potential subjects will be identified after a review of medical records of patients under the care of one or more of the study investigators**
☐	Medical records and/or other Institution sources (databases,registries,billing records,pathology reports,admission logs) will be reviewed to identify potential participants. May involve access of records by individuals not involved in the patient's care.
☐	Potential subjects will be identified by their treating physicians and referred to the researchers. Patients' private and identifiable information will not be shared prior to receiving permission from the patient to do so.
☐	Potential subjects will be identified from a registry of individuals interested in research opportunities.
☐	Subjects will roll-over from another research study.
☐	Potential subjects will self-refer in response to advertisements.

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Interventions and Observations

1.0

Be specific and describe the Interventions or Observations that will be part of this research project. Include a detailed description of the treatment arms, if applicable.

Patient will undergo endotracheal intubation and general anesthesia will be induced using propofol, fentanyl, midazolam, and vecuronium.

All patients will be monitored with standard ASA monitors. An indwelling arterial catheter will be placed, and electrode for the NICOM monitor will be applied. During the procedure, an arterial blood sample will be assessed for blood gas analysis, pH, blood glucose, Hb and lactate.

Once positioned prone, maintenance anesthetic will include 02/Air, diazepam 2 mg/hour up to a maximum total of 10 mg, and an infusion of fentanyl 1 mcg/ kg/hr and ketamine 2 mcg/kg/hr, a loading dose of 1 mcg/kg of dexmedetomidine administered over, plus one of two anesthetic Treatments.

Treatment 1: Propofol 50 mcg/kg/min + dexmedetomidine 0.5 mcg/kg/hr

Treatment 2: Propofol 25 mcg/kg/min + dexmedetomidine 1.0 mcg/kg/hr.

If MEPs are clinically determined to be unmonitorable for patients receiving treatment 2, they will be converted to treatment 1. If MEPs continue to be unmonitorable, anesthetic management will be at the discretion of the attending anesthesiologist. If MEPs are unmonitorable for patient receiving treatment 1, anesthetic management will be at the discretion of the attending anesthesiologist.

Cardiac output will be measured continuously during the procedure. A decrease in cardiac output by 20% or an increase in lactate >2mEq/l will prompt the administration of fluid and/or blood is the Hb is less than 8mg/dl.; to restore the values to baseline. Any deterioration of MEPs will prompt the assessment of metabolic acidosis, cardiac output and Hb level.

Patients may also receive boluses vaso-active medications to control HR and BP.

Motor evoked potentials will be performed in the standard manner. Simulating electrodes will be placed 2 cm anterior to C1 and C3, and C2 and C4 locations of the International 10-20 system. C1 and C3, and C2 and C4 electrodes will be joined using a Y connector, to produce one right and one left cranial electrode. Recording electrodes will be placed in right and left tibialis anterior, abductor hallucis, extensor hallucis longus, medial gastrocnemius, vastus lateralis and rectus femoris muscles. Stimuli will be two sequential trains of 2 then 5 pulses, each pulse 50 microsecond durations, with an inter-pulse intervals of 2 milliseconds and an inter-train interval of 10 and 20 milliseconds. Stimulation voltage will be adjusted to obtain responses in all muscles if possible. MEPs will be performed at standard intervals, typically once every 20 minutes, as permitted by the surgeon.

Additionally, following establishment of stable anesthesia, the stimulation voltage threshold for each muscle will be determined by beginning at 125 volts and increasing at 25 volt increments until a response is obtained in each muscle, and recording the voltage at which the MEP was first recorded

in each muscle.

2.0 Will you be collecting human fluid or tissue? ○ Yes ◉ **No**

If yes, what will you be collecting? ☐ **Fluid** ☐ **Tissue**
(Intraoperative and/or outpatient collection)

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Data Collection

1.0 Indicate what data will be collected.

MEP voltage threshold values for each muscle will be recorded manually.

Timestamped MEP waveform data are recorded and stored automatically by the Cadwell clinical intraoperative monitoring machine.

Timestamped cardiac output data are stored automatically by the NICOM device.

Anesthesia data and blood pressure are stored automatically in EPIC.

Arterial PO2, PCO2, pH, lactate, glucose, and hemoglobin will be sampled and recorded at clinically determined intervals.

2.0 Who will collect the data:

Ronald	Emerson, MD
Michael	Urban, MD PhD

3.0 When the data will be collected? Include timing of visits(either SOC or specifically for the study).

During each surgery

4.0 From what source:

Medical Records

No Private Office Charts Please specify which private office:

No Registries Please specify which registry:

☑ Other Please specify: NICOM and Cadwell Cascade machines

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General Methods and Procedures

1.0 * **Are controls included in the study?** No

1.1 If yes, describe how they will be matched with the study subjects; state whether the controls will have identical data recorded, or describe any differences compared to the intervention subjects.

2.0

* **Are all tests Standard of care?** No

If not, identify which tests are not standard of care. What source of funds will be used to pay for them (text box below):

Use of the NICOM monitor is not standard of care at HSS, but HSS does own a NICOM monitor. There will be charge to the patient for its use.

3.0 * **Will surveys/questionnaires be used?** No

4.0 * **Does the study involve randomization?** Yes

5.0 * **Does your study included Placebo or No-Treatment Arm?** No

6.0 * **Does your study included Washout of Previous Medication?**
No

7.0 Data collection sheet should be created for the study and uploaded:

Name	Version
There are no items to display	

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Randomization

1.0 Please state who will do the Randomization:

The randomization schedule will be generated by a member of the Healthcare Research Institute not otherwise involved in the trial.

2.0 Please state when the Randomization will be done:

The randomization schedule will be generated prior to the start of study enrollment.

After consent is obtained, the anesthesiologist will be given a sealed opaque envelope corresponding to the patients study ID number and randomized to one of the two treatment groups. The envelope will be opened in the operating room, not in the presence of other investigators.

3.0 Please state how the Randomization will be performed:

A Healthcare Research Institute member not otherwise involved in the trial will prepare the randomization schedule using SAS software. Group assignment will be indicated on cards within numbered sealed opaque envelopes. The envelopes will be prepared by a staff member not otherwise involved in the trial.

4.0 Please state who will insure that the Randomization is carried out and if anyone will be blinded to the Randomization group:

All investigators except for the anesthesiologist will be blind to the randomization group.

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Sample Size and Data Analysis

If you are uncertain about how to calculate your sample size and determine appropriate data analysis, please contact the Epidemiology and Biostatistics Core at biostats@hss.edu for assistance in completing this section.

1.0 Is this is a case series based only on the patients available using descriptive statistics in lieu of a sample size calculation?

* No

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Sample Size and Data Analysis

Support estimates with evidence from the literature of prior studies and perform an appropriate sample size calculation.

For hypothesis testing (e.g., the calculation of p-values using statistical tests), you need to estimate your available sample size and calculate the effect size that will be detectable using your proposed statistical analysis plan. This also applies to a case series where you plan hypothesis testing.

1.0 If you have consulted with a statistician, please indicate their name:

Kara Fields

2.0 Proposed sample size analysis, include the following:

- **Student's t-test, ANOVA, chi-square, regression, etc;**
- **Alpha level;**
- **Beta or power level;**
- **Primary outcome variable estimate (mean +/-s.d. for continuous outcome, frequency/percentage for categorical variable);**
- **Number of groups being compared (use 1 for paired analysis within the same subjects);**
- **Effect size or change expected between groups;**
- **Resulting number per group**

1. **Proposed analysis (e.g., student's t-test, ANOVA, chi-square, regression, etc.):** Fisher's exact test
2. **Alpha level:** 0.05 (two-sided)
3. **Beta or power level:** 80% power
4. **Primary outcome variable estimate (mean +/- s.d. for continuous outcome, frequency/percentage for categorical variable):**

   Percentage of patients with monitorable MEPs for the purpose of monitoring spinal cord integrity in 0.5 ug/kg/hr dexmedetomidine group = 100% *. Percentage of patients with monitorable MEPs for the purpose of monitoring spinal cord integrity in 1.0 ug/kg/hr dexmedetomidine group = 75%.

5. **Number of groups being compared (use 1 for paired analysis within the same subjects):** 2
6. **Effect size or change expected between groups:** 25 percentage point difference
7. **Resulting number per group:** 31

Total sample size required: 62 + 10% to account for missing/unusable data = 68

* Li Y, Meng L, Peng Y. Effects of Dexmedetomidine on motor- and somatosensory-evoked potentials in patients with thoracic spinal cord tumor: a randomized controlled trial. BMC Anesthesia. 2016;16:51. DOI 10.1186/s12871-016-0217-y

3.0 Data Analysis: describe how the primary outcome will be

analyzed and what types of statistical calculations will be used. Do the same for each secondary outcome. Reiterate briefly the main analysis to be done, which groups, which variables, possible confounders. Address how possible confounders will be identified and handled in analysis:

The percentage of patients with monitorable MEPs for the purpose of monitoring spinal cord integrity present at all assessments (yes vs. no), the primary outcome, will be compared between groups using Fisher's exact test.

The percentage of patients in each group with monitorable MEPs for the purpose of monitoring nerve root integrity present at all assessments (yes vs. no) will be presented as risk difference and relative risk with 95% confidence intervals.

The correlation between MEP metrics (peak to peak amplitude, waveform integral, waveform line-length, trial variability of peak to peak amplitude, trial variability of waveform integral, and trial variability of waveform line-length) and CO over time will be assessed via mixed modeling. Correlation coefficients will be presented as point estimates along with 95% bootstrap confidence intervals.

Balance on demographics and baseline characteristics will be assessed by calculating standardized differences (difference in means or proportions divided by the pooled standard deviation) between groups. Balance will be assessed using two thresholds: (1) $1.96 \times (2/34)^{1/2} = 0.475$ and (2) 0.2 (Austin 2009).

References

1. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. Stat Med 2009; 28: 3083-107.

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Consent Information

1.0 Describe how, when, and where the consent process will be initiated:

Informed consent will be obtained in the holding area, prior to surgery, by the principal investigator or an IRB approved co-investigator

2.0 Who will obtain informed consent from subjects for this research?

First Name	Middle Name	Last Name	Title
Ronald		Emerson, MD	

Michael Urban, MD PhD

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You have completed the Clinical Research Proposal for this study. Click FINISH button to save and exit the proposal.

When you are ready to submit your proposal for pre-review, hit the SUBMIT STUDY link on your study homepage. The appropriate Clinical Review Panel (CRP) will receive and review your proposal.

Should you have any questions, please contact Barbara Bosco at 212.606.1914.