Massachusetts Eye and Ear

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CLINICAL RESEARCH PROTOCOL

PI Name: Martha Cordoba, M.D	**Date:** 05/01/2017
IRBNet ID: 1047249	**Protocol Version Number/Date:**
Protocol Title: Perioperative complications of deep extubation in adults undergoing head and neck surgery at Massachusetts Eye and Ear Infirmary.	

Use this protocol for prospective clinical research studies that are not clinical trials.

1. STUDY SUMMARY

Provide a brief summary of the proposed research (in language that can be understood by a non-scientist).

Response:
We propose a prospective observational cohort study in order to investigate the perioperative respiratory complications of deep extubation in adults undergoing head and neck surgery at Massachusetts Eye and Ear. Data pertaining to perioperative respiratory complications from adult patients presenting to MEE for head and neck surgery who undergo deep extubation will be collected for this study.

2. SPECIFIC AIMS

List the specific aim(s) and objective (s) of the study (i.e., what does the study hope to accomplish). Include any secondary and exploratory aims and objectives (e.g., biomarkers, genetic analyses).

Response: To assess the perioperative respiratory complications rate of deep extubation in adult patients undergoing head and neck surgery at MEE.

3. BACKGROUND AND SIGNIFICANCE

Describe the scientific background and rationale for the study.

- Provide a critical review of the relevant literature and the state of current knowledge on the topic. Discuss deficiencies or gaps in knowledge that make the study worth doing. Include a list of literature cited in an appendix at the end of this protocol.
- Discuss the importance of the topic with respect to scientific knowledge, clinical practice, public health, impact on individuals/community, incidence, prevalence, mortality and morbidity, as applicable.

Response:

Tracheal extubation in patients undergoing head and neck surgery may be followed by several respiratory complications, such as coughing, desaturation, laryngospasm, bronchospasm, and airway obstructions.[1, 2] The trachea can be extubated when the patient is still deeply anaesthetized or after he/she fully regains consciousness. Currently, the default method of extubation at Massachusetts Eye and Ear Infirmary (MEEI) is deep extubation. In contrast, the default method of extubation in most centers in the United States is awake extubation.

Respiratory complications may occur following both deep and awake extubation, and the superiority of one method over another has not been established. When the trachea is extubated in light stages of anesthesia or after the patient has regained consciousness, there can be significant increases in heart rate and arterial pressure that may continue into the recovery period. This increase in blood pressure and heart rate may be partially due to straining during extubation. In patients in whom these stimulatory effects can be detrimental, tracheal extubation under deep anesthesia may reduce the incidence and degree of these complications; however, tracheal extubation under deep anesthesia may cause respiratory complications, including laryngospasm, bronchospasm, and negative pressure pulmonary edema.[3]

There is a paucity of research related to deep or awake extubation in adults. Specifically, such studies are lacking in patients who undergo head and neck surgery. In a prospective survey of respiratory complications of tracheal intubation and extubation of 1005 patients 16 years or older who underwent elective general anesthesia, Asai et al found that the incidence of respiratory complications was higher in the deep versus the awake extubation group, regardless of the type of operation.[3]

However, studies in the pediatric population have shown a different picture. In children undergoing adenotonsillectomy, von Ungern-Sternberg et al have shown that patients who were extubated while awake had a higher incidence of severe coughing and desaturation at emergence, as well as a higher rate of hoarse voice on the first postoperative day.[4] Although there was no difference in the instances of oxygen desaturation between the two methods of extubation, these episodes tended to be more common and of longer duration in the awake group. In contrast, the children who were extubated while deeply anaesthetized showed an overall higher incidence of partial airway obstruction.

Given the serious nature of untoward respiratory events in the perioperative period associated with tracheal extubation, we propose a prospective observational cohort study to further assess the perioperative respiratory complications of deep extubation, the default method of extubation at MEE in adults undergoing head and neck surgery.

References:

1- Miller KA, Harkin CP, Bailey PL. Postoperative tracheal extubation. Anesth Analg 1995; 80: 149–72.

2- Hartley M, Vaughan RS. Problems associated with tracheal extubation. Br J Anaesth 1993; 71: 561–8.

3- Asai T, Koga K, Vaughan RS, et al. Respiratory complications associated with tracheal intubation and extubation. Br. J. Anesth. 1998, 80, 767–775.

4- Ungern-Sternberg BS, Davies K, Hegarty M, et al. The effect of deep vs. awake extubation on respiratory complications in high-risk children undergoing adenotonsillectomy. Eur J Anaesthesiol 2013; 30: 529–536.

4. STUDY DESIGN

Provide a detailed description of the study design (e.g. cross-sectional, stratified, longitudinal, prospective cohort, case-control, randomized, placebo-controlled, masked/double masked, feasibility, pilot, proof-of-concept, etc.).
Explain why this study design is appropriate for this study.

Response:

Our study is a prospective observational cohort study. We will record the respiratory complications, such as bronchospasm, laryngospasm, respiratory depression, desaturation, persistent cough, and apnea after deep extubation in patients undergoing head and neck surgery at MEE.

We will also collect following data:

1) Length of time from the end of surgery to leaving the OR;
2) Length of stay from admission to the PACU to discharge home;
3) Any unplanned hospital admission due to perioperative respiratory adverse events.

5. SUBJECT INFORMATION

a) Target Enrollment- Specify the number of subjects you plan to enroll and justify why this number is sufficient to achieve adequate power for statistical analysis taking into account anticipated screen failures and drop-outs. Include sample size by cohort if the study has multiple cohorts.

Response: Our proposed sample size of 300 patients will enable us to report the complication rates with adequate precision in terms of a sufficiently narrow two-sided 95% confidence interval. For example, if the observed respiratory complication rate is 30%, as was reported by Asai T et al (1), our confidence interval will have a half-width of 5%. If a complication rate that we observe is 35%, the half-width of our confidence interval will be 6% (nQuery Advisor version 7). We have used nQuery Advisor version 7 for the calculation of our sample size. For a CI of 95%, $\alpha = 0.05$, P= 80%, and a complication rate of deep extubation of 30%, as reported by Asai T et al (Asai T, Koga K, Vaughan RS, et al. Respiratory complications associated with tracheal intubation and extubation. Br. J. Anesth. 1998, 80, 767–775.), we will require a sample size of 300.

1) Asai T, Koga K, Vaughan RS, et al. Respiratory complications associated with tracheal intubation and extubation. Br. J. Anesth. 1998, 80, 767–775.

b) If this is a multi-center study and other sites rely on the MEE HSC as the IRB of record, please specify the total number of subjects required by all sites to achieve sufficient power.

Response: N/A

c) Provide justification that the researchers have access to sufficient numbers of eligible subjects to meet target enrollment goals (e.g., researcher's own patients, clinic patients with a specific diagnosis, subjects from previous studies who agree to participate in future studies).

Response: Potentially eligible subjects for this study are all adult patients who undergo head and neck surgery as well as deep extubation at the end of the surgery per the discretion of the anesthesiologist assigned to the case. Deep extubation is the default extubation method practiced at MEE. Therefore, there will be a sufficient number of potentially eligible subjects to meet the target enrollment goals.

6. ELIGIBILITY CRITERIA

a) Inclusion Criteria - Inclusion criteria are the specific characteristics of the study population(s) required for study enrollment (e.g., ages, gender, condition or disease.) List the inclusion criteria in a bulleted list.

Response: Adult men and women who present to MEE for head and neck surgery and undergo deep extubation will be included.

b) Exclusion Criteria - Provide specific criteria for determining ineligibility to participate. Provide justification for their exclusion (e.g., pregnant women).

Note: Exclusion criteria are not always clinical in nature. Exclusion may also include circumstances that interfere with:

- the participant's ability to give informed consent (diminished cognitive capacity or a language other than English and an interpreter unavailable)
- contraindications to the study treatment(s)/procedure(s)
- taking certain concomitant medication(s) or
- conditions that interfere with a patient's ability to comply with all study procedure(s)

Response: We do not exclude anyone from the study.

NOTE: Per federal regulations, the risks and benefits of research must be fairly distributed among the populations that could benefit from the research. No groups of persons (e.g., gender, pregnant women, children, minorities, non-English speakers) should be categorically excluded from research without a valid scientific or ethical reason to exclude such groups.

c) Describe your rationale that the study population is representative of populations that may potentially benefit from the research, or the rationale for excluding certain groups, if applicable.

Response: N/A

7. RECRUITMENT PROCESS

NOTE: HIPAA does not permit non-MEE physicians to disclose patient information to Mass Eye and Ear for research recruitment. Non-MEE physicians may inform their patients of a research study and allow the patients to self-disclose their interest to the MEE study team.

Provide a detailed description of the recruitment plan (consistent with information you provide in the PRA), who is responsible for recruitment, how and when subjects will be recruited (i.e., flyers, advertisements, letters and oral/telephone scripts, email, at clinic appointments, etc.). Note: The HSC must review all recruitment materials. Please upload these materials into IRBNet with this submission.

Response: All adult patients who undergo head and neck surgery as well as deep extubation at the end of the surgery will be eligible for this study. The protected health information, including only names, MRN, and Date of surgeries of all eligible patients will be accessed from Epic at the screening process. We will not use email, fliers or brochures to recruit subjects. All surgeons performing head and neck surgery and all anesthesiologists at MEE will be notified of and informed about the study. Upon arrival to the preoperative area at MEE two hours prior to surgery, patients will be registered and seen by the preoperative nurse. Afterwards, an anesthesiologist will perform the preoperative evaluation. A data-recording form will be handed to the anesthesiologist in order to collect all the information requested in the form for patients undergoing deep extubation at the end of the surgery. The investigator and study coordinator will monitor the data collecting.

8. CONSENT PROCESS

a) 8a. Describe the consent process in detail. Include the following information:
   - who (e.g., physician, nurse, coordinator) will obtain consent,
   - their knowledge/experience in obtaining consent
   - location of the consent process
   - use of the Documentation of Consent Process Form
   - how the study information is presented (written consent form, orally, study information sheet, use of "short form" or translated consent etc.)
   - timing of consent (e.g., during pre-surgical visit, about one week before the screening visit)

Response: We request a waiver of informed consent from the HSC.

b) 8b. How will you assess a subject's understanding of the research initially and over the course of the study? Is the presentation of study information appropriate for the study population (low vision, hearing impaired)? Describe specific provisions for subjects with limited understanding (e.g., a family member or other appropriate 3rd party is involved in the consent process).

Response: N/A

c) 8c. If the research-related intervention or interaction will occur on the same day that the subject initially receives information about the study, justify why this is appropriate/necessary.

Response: N/A

d) 8d. Describe provisions in place for non-English speaking subjects (view guidance on the HRPP Sharepoint Site http://sharepoint/departments/research/HumanResearch/SitePages/Home.aspx), including use of translators during the consent process and the translation of consent documents.

Response: N/A

e) 8e. If a subject cannot read the consent form (e.g., low literacy, low or no vision) or cannot hear the person obtaining consent, explain how you will conduct the consent process and the provisions to accommodate subjects with limited or no hearing and/or limited or no vision.

Response: N/A

9. STUDY PROCEDURES

a) Provide a detailed description of all study procedures and intervention(s) each subject and/or cohort will experience. Provide a schedule of visits and the procedures that occur at each visit (e.g., tests, questionnaires, surveys, imaging or other interventions.). If the study also involves standard of care, differentiate between research only procedures and standard of care.

Response**:**

Preoperative Phase	• Research only: All surgeons who perform head and neck surgery at MEE will be notified of and informed about the study. • Upon arrival to the preoperative area at MEE two hours prior to surgery, patients will be registered and then seen by the preoperative nurse. • Next, an anesthesiologist will perform the preoperative evaluation. • Women aged 18 years and older will be offered a pregnancy test screening. • An IV catheter will be placed in all patients in the preoperative holding area on the surgical floor. • Research only: A data-recording form will be handed to the anesthesiologist. • Research only: The anesthesiologist will fill out data sheet questions related to patient's past medical history from the anesthesia preoperative evaluation form. • Research only: The data-recording form will include multiple parameters that will be recorded in the perioperative period to quantify any adverse respiratory events including: 1. Oxygen saturation at the following intervals: 5 minutes prior to extubation; immediately before extubation; every minute for the first 10 minutes following extubation, except during transport to the PACU; and subsequently, every 5 minutes for the ensuing 30 minutes; 2. Endtidal CO_2 at the time of extubation; 3. Desaturation to less than 95% for more than 10 seconds; 4. Type and amount of opiates administered during the surgery; 5. Time from the end of the surgery to leaving the OR;

		6. Systolic and diastolic blood pressure and heart rate at the time of extubation, as well as upon arrival in the PACU, and subsequently, every 5 minutes for the first 30 minutes; 7. Episodes of persistent cough, defined as 3 or more consecutive coughs; 8. Episodes of complete or partial laryngospasm; 9. Episodes of bronchospasm; 10. Incidence of negative pressure pulmonary edema; 11. Incidence of vomiting; 12. Incidence and type of airway interventions; 13. Episodes of apnea; 14. Type and amount of opiates administered during the PACU stay; 15. Length of stay in minutes from admission to the PACU to discharge home; 16. Any unplanned hospital admissions due to perioperative respiratory adverse events;
	Intraoperative Phase	• Standard ASA monitors, including pulse-oximetry, ECG, non-invasive blood pressure, thermometer, and capnography, will be applied in all patients. • All patients will be preoxygenated prior to induction. • **Induction:** o The choice of induction drugs will be at the discretion of the anesthesiologist. • **Maintenance:** o The choice of maintenance drugs, including choice and dose of opiates, will be at the discretion of the anesthesiologist. • **Emergence and extubation:** o The choice extubation method (deep vs awake) will be at the discretion of the anesthesiologist.

	○ Deep extubation criteria will be at the discretion of the anesthesiologist. ○ An oral or nasal airway will be placed in patients immediately after deep extubation.
Postoperative Phase	• All patients will be transported to the post-anesthesia care unit (PACU) with a facemask receiving oxygen. • The anesthesiologist will remain with the patient until he/she is stable enough be handed off to the PACU nurse. • Patients will be continued on supplemental oxygen until fully awake; they will be placed on room air when able to maintain adequate oxygen saturation as assessed by the PACU nurse. • Research only: The data-recording form will be handed to data recorder in the PACU to be completed.
Discharge	Patients will be discharged home or to the floor after meeting PACU discharge criteria.
Analysis	Research only: The data will be analyzed and reported.

b) 9b. Describe any data and/or sample banking, if applicable.

Response: N/A

c) 9c. If the study includes randomization describe the randomization process and randomization ratio, (include block size, permutations and stratification, if applicable.).

Response: N/A

d) If there are circumstances under which the researcher may withdraw participants, describe the conditions and process for withdrawal. Describe how subjects can withdraw from the study (e.g., calling or emailing the investigator/study coordinator).

Response: N/A

10. STUDY OUTCOMES

a) **Primary Outcome Measure(s)** - describe how you will measure the primary and other outcomes of the study (e.g., blood pressure change, changes in visual acuity using a specific test, pain scales, responses on a questionnaire, etc.). Upload copies of your data collection tools and/or a list of all variables/data points you will collect.

Note: Primary outcome measures may be measured in various ways such as:

- binary (e.g. improvement in symptoms vs. no improvement in symptoms)
- continuous (e.g. weight - kg, blood loss - mL)
- ordinal (e.g. pain - mild, moderate, severe)
- time to event (e.g. survival)
- counts (e.g. number of infections, number of events occurring)

Response:
Primary outcome measures include:

1) Desaturation to less than 95% for more than 10 seconds;
2) Episodes of persistent cough, defined as 3 or more consecutive coughs;
3) Episodes of complete or partial laryngospasm;
4) Episodes of bronchospasm;
5) Incidence of negative pressure pulmonary edema;
6) Obstruction that requires maneuvers, oral airway or jaw thrust

b) Describe any secondary or other outcomes (exploratory):

Secondary outcome measures include:

1) Length of time from end of surgery to leaving the operating room;
2) Length of stay from admission to and discharge from the PACU Stage 1 and 2;
3) Incidence of unexpected hospital stay related to perioperative respiratory complications.
4) Incidence of sore throat

11. HYPOTHESES

Hypotheses are more specific than specific aims and are tested using predetermined statistical methods and form the basis for statistical power calculations. The primary hypothesis is a statement of the effect of the research intervention/interaction on the primary outcome measure. Hypotheses are generally stated as the null and alternative hypotheses (H0, Ha) as they have their basis in inferential statistics. Rejecting the null hypothesis with a specific level of probability indicates that there is a relationship between the variables being studied. State the alternative hypothesis which you expect your data to support.
Examples of null and alternative hypotheses

- H0: Chronic sinusitis prevalence rates are not different among children from low and high socioeconomic groups
- Ha: Chronic sinusitis prevalence rates are different among children from low and high socioeconomic groups.

a) Describe the primary hypothesis:

Response:

H0: The rate of perioperative respiratory complications of deep extubation in adults undergoing head and neck surgery at MEE is not different among other institutions.

Ha: The rate of perioperative respiratory complications of deep extubation in adults undergoing head and neck surgery at MEE is different than other institutions.

b) Describe any secondary hypotheses.

Response:
1) Length of time from end of surgery to leaving the operating room;
2) Length of stay from admission to and discharge from the PACU Stage 1 and 2;
3) Incidence of unexpected hospital stay related to perioperative respiratory complications.
4) Incidence of sore throat.

Is there a significant association between the lengths of time from end of surgery to leaving the operating room with the perioperative respiratory complications?

Is there a significant relationship between the lengths of stay from admission to and discharge from the PACU?

What is the incidence of unexpected hospital stay associated with perioperative respiratory complications?

What is the incidence of sore throat?

12. STATISTICAL METHODS

Describe the planned statistical methods including specific tests (e.g., parametric and non-parametric tests, estimation of incidence and prevalence rates, odds ratios, survival/failure analyses, intent to treat analyses). Provide the power calculations used to estimate the proposed sample size. If needed, please consult a biostatistician. (Note: Biostatistical consults are available through Harvard Catalyst.)

Response:
Our proposed sample size of 300 patients will enable us to report the complication rates with adequate precision in terms of a sufficiently narrow two-sided 95% confidence interval. For example, if the observed respiratory complication rate is 30%, as was reported by Asai T et al (1), our confidence interval will have a half-width of 5%. If a complication rate that we observe is 35%, the half-width of our confidence interval will be 6% (nQuery Advisor version 7). We have used nQuery Advisor version 7 for the calculation of our sample size. For a CI of 95%, $\alpha = 0.05$, P= 80%, and a complication rate of deep extubation of 30%, as reported by Asai T et al (Asai T, Koga K, Vaughan RS, et al. Respiratory complications associated with tracheal intubation and extubation. Br. J. Anesth. 1998, 80, 767–775.), we will require a sample size of 300.

1) Asai T, Koga K, Vaughan RS, et al. Respiratory complications associated with tracheal intubation and extubation. Br. J. Anesth. 1998, 80, 767–775.

13. RISKS AND DISCOMFORTS AND MINIMIZATION OF RISKS

Risk *is the probability and magnitude of harm or discomfort anticipated as a result of participation in the research.*
Minimal risk *means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.*

a) Describe any risks of harm to subjects and/or anticipated discomfort(s) that are reasonably foreseeable, even if unlikely. Identify the safeguards you will put in place to minimize the occurrence of these risks and discomforts. Risks of harm and discomfort may include: physical harm/discomfort, psychological harm/discomfort, legal harm/discomfort, social harm/discomfort and economic harm.

Response: There are two methods of extubation in patients undergoing anesthesia: deep or awake. Currently, deep extubation is the default extubation method at MEE. However, in almost every other institution in the country, awake extubation is the default method. Risks of airway complications are associated with both methods and can include the following: 1) desaturation and hypoxia; 2) partial or complete laryngospasm; 3) bronchospasm; and 4) negative pressure pulmonary edema. Since this study is observational, there will be no risk for patients accruing from participating in the study. Recording of additional data by the anesthesiologist assigned to the case after extubation will not impact clinical care of the patient as the anesthesiologist will be monitoring the same vital signs whether the patient is part of the study or not. The computerized anesthesia manager program captures all the vital signs until the patient is disconnected and transported to the PACU. In the PACU, the data

recorder will be recording the additional data. The only document with the patient's identifiers will be the data sheet, which will be filled out by the anesthesiologist during the case and by the data recorder in the PACU. Subsequently, all data will be recorded as a research record on an MEE password protected computer. Patient's data sheets will be locked in the drawers located in the anesthesia office on the 7th floor of the MEE main building. Only the study coordinator and the principal investigator have access to these drawers. Consequently, the patients' data will remain confidential all the time.

b) If applicable, describe any group harms (i.e. research that focuses on a specific group or population that if the results are disclosed, could harm the group as a whole).

Response**: N/A**

c) Describe any anticipated circumstances in which a "breach of confidentiality" associated with a mandated disclosure (e.g. reporting abuse to authorities) may occur as part of this study?

Response**: N/A**

d) What risk classification (taking into consideration the probability and magnitude of harm) is appropriate for the proposed research?

☒ Minimal Risk ☐Greater than Minimal Risk ☐ Unknown

e) Explain why you feel this category is appropriate based on the definition above (if more than minimal risk, describe the likelihood and seriousness of such risks).

Response**:** This study is an observational study; thus, there will be no intervention. The deep extubation is a method of extubation used for patients for any type of surgery. After transport to the PACU, the anesthesiologist routinely stays with the patient until it is safe to hand the patient off to a PACU nurse.

14. ALTERNATIVES

Describe any alternatives, to research participation available to potential patients.

Note: If there are no alternatives, other than "not participate" state so.

Response**: N/A**

15. BENEFITS

a) Will individual subjects have any direct benefits from the research? If subjects will not experience direct benefit, state so.

Response: Subjects will not receive any direct benefits.

b) Explain the potential benefits to science, and/or society as a result of this research.

Response: As deep extubation is the default method at MEEI, our study might be able to illustrate and elucidate the safety features as well as the rate of different respiratory complications of the deep extubation in adult patients undergoing head and neck surgery.

c) If this study is more than minimal risk, explain how the risks are minimized in relation to the anticipated benefits of the study:

Response: N/A

16. DISSEMINATION OF RESULTS

a) Describe any plans to share research results with subjects, EITHER individual results and/or aggregate results. If there are no plans to share results, explain why this is not feasible, appropriate, or applicable to this research.

Response: N/A – This study is exempt from obtaining consent from patients as the nature of this study is observational and we collect very minimal patient identifiers. Also, all patients' data being collected and analyzed in this study are de-identified.

b) How will results be published, and in what form (newsletter to subjects, peer-reviewed publications)?

Response: The results of this study will be published on peer-reviewed medical journals. Subjects will not be individually identifiable in publications.

17. INCIDENTAL FINDINGS

If there is the possibility that study procedures may identify incidental findings of medical importance to a subject and/or the subject's family (e.g., genetic studies, imaging studies, studies that conduct routine blood tests, etc.), describe the plan for reporting any incidental findings (e.g., study physician will discuss with subject/subject's PCP, genetic counseling). In addition, researchers may uncover evidence of child, domestic, or elder abuse, which require reporting to authorities. Please describe the plan for reporting such findings.

Response: There will not be a possibility of clinically significant incidental findings being discovered during research procedures as this study is clinical research

18. PRIVACY/CONFIDENTIALITY

NOTE: MEE researchers must adhere to MEE Information Security Policies and Procedures when designing their research protocols. The HSC evaluates the collection, use and storage of data and may require additional safeguards. For example, the HSC may require a Certificate of Confidentiality for research projects that collect personally identifiable, sensitive information.

a) Describe the plan for protecting the privacy and confidentiality of subjects throughout the research (e.g., limited access to medical records and identifiable study data, data security procedures consistent with MEE Information Security Policy).

Response: Research data will be coded using a subject identification number that does not include the subject's initials and is not derived from the subject's identifiable information. The key linking the subject identification number to the subject's identifiable information (only MRN) is available only to Mass. Eye and Ear PI and other MEE study team members.

b) Where will you store research data, signed informed consent forms, and assent forms to maximally protect privacy and confidentiality?

Response: Response: Paper files will be locked in cabinets when not in use and protected from inappropriate access. Electronic data will be stored in a password protected file and networked MEE computer for which access is limited to authorized members of the study team only.

c) Please provide the plan for destroying identifiers (at the earliest opportunity as consistent with the research plan) or provide a health or research justification for retaining identifiers. For protocols subject to future and secondary data analysis, provide justification for not destroying identifiers permanently and explain plans for future use (i.e., establishment of a data or specimen repository).

Response: Identifiers will be destroyed after the publication of the study

d) Will you obtain samples/data from outside sources? Please specify from whom you will obtain samples and what information you will obtain with each sample. Please note that a Material Transfer Agreement may be required for this research activity. (Contact Research Administration for instructions.)

Response: No

e) Will samples from MEE be provided to outside sources? Please specify to whom you will provide MEE samples and what information/data will accompany each sample. Please note that that a Material Transfer Agreement will be required for this research activity.

Response: No

19. DATA and SAFETY MONITORING PLAN (DSMP)

a) If the research is no more than minimal risk, describe any provisions in place to ensure the safety of participants. In minimal risk studies, there is always the risk of loss of confidentiality and privacy. However, minimal risk studies involving blood draws, imaging, and eye exams may have risks associated with the study procedure.

Response: Risks of airway complications are associated with both awake and deep extubation methods and can include the following: 1) desaturation and hypoxia; 2) partial or complete laryngospasm; 3) bronchospasm; and 4) negative pressure pulmonary edema. Since this study is observational, there will be no risk for patients accruing from participating in the study. Recording of additional data by the anesthesiologist assigned to the case after extubation will not impact clinical care of the patient as the anesthesiologist will be monitoring the same vital signs whether the patient is part of the study or not. The computerized anesthesia manager program captures all the vital signs until the patient is disconnected and transported to the PACU. In the PACU, the data recorder will be recording the additional data. The only document with the patient's identifiers will be the data sheet, which will be filled out by the anesthesiologist during the case and by the data recorder in the PACU. Subsequently, all data will be recorded as a research record on an MEE password protected computer. Patient's data sheets will be locked in the drawers located in the anesthesia office on the 7th floor of the MEEI main building. Only the study coordinator and the principal investigator have access to these drawers. Consequently, the patients' data will remain confidential all the time.

b) If the research is more than minimal risk, please provide a detailed data and safety monitoring plan (DSMP). Include the individual(s) or group responsible for data and safety monitoring (e.g., PI, specific members of the study team, independent monitor(s), a convened Data and Safety Monitoring Board - DSMB) Please see the guidance document in IRBNet for developing a DSMP.

Response: N/A

c) Provide information related to the expertise and qualifications of the individual(s) and/or groups listed above relative to monitoring.

Response**: N/A**

d) Please explain how data and safety monitoring activities for this study will be documented (e.g., a monitoring log kept in the regulatory binder).

Response**: N/A**

e) Explain if any individual involved in monitoring has relationships with sponsors, organizers or researchers, conducting the study, and if applicable, describe the nature of these relationships.

Response**: N/A**

f) If applicable, describe the process for communication of Data and Safety Monitoring Board reports to the investigator and to the HSC.

Response**: N/A**

20. DATA REVIEW AND QUALITY ASSURANCE

a) Specify the frequency of data review (a specific number of times, at defined time points, after enrollment of a certain number of subjects, or as needed).

Response**: There will be an interim analysis after half of the study subjects have been enrolled.**

b) Who will be responsible for data review (e.g., PI, study staff)? If data review is shared, describe each person(s) or group responsibility.

Response**:** The study coordinator Alex Ciaramella will be responsible for data review and compilation.

c) If applicable, please describe the electronic data capture systems you will use and describe the training provided for those who will use these systems.

Response**: Epic is used to store patient information at MEE, Alex Ciaramella has been taught as per company policy on how to use this program.**

d) What processes are in place for addressing unresolved or significant issues (e.g., significant noncompliance with the protocol) identified by data review at MEE (or across study sites, when applicable)?

Response**: N/A**

21. ADVERSE EVENTS

a) Describe how and by whom adverse events will be identified.

Response**: N/A -**

b) Describe any "drop criteria" for individual research subjects who experience an adverse event including who will be responsible for making these determinations.

Response**: N/A**

c) Describe any "stopping rules" for parts of the study, or for the entire study due to adverse events including who will be responsible for making these determinations.

Response**: N/A**

d) Please acknowledge and state that adverse events and unanticipated problems will be reported to the HSC in accordance with the HSC policy on Reporting Adverse Events and Unanticipated Problems.

Response**: N/A**