**DEFENSE HEALTH AGENCY**
NAVAL MEDICAL CENTER
620 JOHN PAUL JONES CIRCLE
PORTSMOUTH, VIRGINIA 23708-2197

April 28, 2025

MEMORANDUM

From: DHA IRB Office at Naval Medical Center Portsmouth
To: CDR Michael Lee

Subj: APPROVAL OF NMCCL.2025.0007 "A SINGLE-CENTER, PATIENT- AND ASSESSOR-BLINDED, RANDOMIZED CONTROLLED TRIAL TO COMPARE PATIENT OUTCOMES BETWEEN DEFLATED AND INFLATED CUFF ENDOTRACHEAL EXTUBATIONS PROCEEDING SCHEDULED, NON-AIRWAY SURGERY IN HEALTHY ADULTS (DICEE)"

Ref: (a) Code of Federal Regulations, Title 32
(b) DoDI 3216.02 "Protection of Human Subjects and Adherence to Ethical Standards in DoD-Conducted and -Supported Research", April 2020, as amended.
(c) Code of Federal Regulations, Title 45, Part 164

1. Submission. A new protocol (EIRB Reference: 975945) was submitted to NMCCL HRPP on 08/23/2024, completed NMCCL scientific review on10/19/2024, and was submitted to the NMCP IRB on 10/22/2024.

2. Approval. Naval Medical Center Portsmouth (NMCP) IRB-2 reviewed NMCCL.2025.0007 "A single-center, patient- and assessor-blinded, randomized controlled trial to compare patient outcomes between Deflated and Inflated Cuff Endotracheal Extubations proceeding scheduled, non-airway surgery in healthy adults (DICEE)" and approved on **04/24/2025**.

3. IRB Determinations. The following determinations were made in accordance with references (a) through (c) as part of this approval:

a. Approval Category(ies). The above referenced study is Full Board.

b. Risk Assessment. The above referenced study has been assigned a risk rating of Greater than Minimal Risk 32 CFR 219 / 21 CFR 56

c. Enrollment. The study is approved for 88 subjects.

d. Study Expiration. The above referenced study has been approved for a period of one year minus one day, with an expiration date of **04/23/2026.** Naval Medical Center Portsmouth IRBs are continuing to require continuing reviews for non-exempt human subjects research protocols due to the transient nature of base personnel.

e. Informed Consent. An informed consent process encompassing all the required elements of informed consent IAW 32 CFR 219.116 has been approved. Investigators must use the stamped IRB-approved consent form. Federal regulations require that each subject receive a copy of the consent document.

f. HIPAA Authorization. A compound Health Insurance Portability and Accountability Act (HIPAA) Authorization has been approved as part of the stamped, IRB-approved consent form. Federal regulations require that each subject receive a copy of the consent document.

The request for a partial waiver of Health Insurance Portability and Accountability Act (HIPAA) Authorization to use or disclose protected health information (PHI) for research screening purposes has been approved, in accordance with 45 CFR 164.152, as the use or disclosure of PHI involves no more than minimal risk to the privacy of the individuals, 2) the research could not practicably be conducted without the waiver or alteration, and 3) the research could not practicably be conducted without access to and use of PHI.

4. Approved Documents. Approval of the above referenced study includes the following documentation:

| Submission Components Approved | | |
|---|---|---|
| Document Type | Version | Date Approved |
| EIRB Protocol Template | Version 1.5 | |
| Perioperative DCT | Version 1.2 | 04/24/2025 |
| Post-op Symptom Diary | Version 1.1 | 04/24/2025 |
| Post Op Telephone or in Person Script and DCT | Version 1.2 | 04/24/2025 |
| Telephone Recruitment Script | Version 1.2 | 04/24/2025 |
| Subject ID Log | Version 1.0 | 04/24/2025 |
| Data Spreadsheet | Version 1.0 | 04/24/2025 |
| Adverse Events log | Version 1.0 | 04/24/2025 |
| Waiver of HIPAA Authorization for screening purposes only | Version 1.0 | 04/24/2025 |
| NMCCL.2025.0007 DHA ICF and HIPAA | Version 1.3 | 04/24/2025 |

5. Agreements. It is the Principal Investigator's (PI's) responsibility to obtain necessary approvals from other offices, such as the DHA Privacy Office, Technology Transfer Office, and/or Information Management Control Office, before initiating or continuing research.

6. Protocol Registration. If indicated in the study protocol, it is the PI's responsibility to register the study with Defense Technical Information Center (DTIC) (https://discover.dtic.mil) and/or www.ClinicalTrials.gov as soon as possible.

7. Post-approval Requirements. Post-approval study actions must be submitted in EIRB (https://eirb.csd.disa.mil) by the PI.

a. Continuing Review. The study expiration date is **04/23/2026**. The IRB Office strongly recommends that continuing reviews are submitted at least sixty days prior to study expiration. If the study expires, the IRB Office will notify study investigators that all study activities must be suspended, and the IRB will take steps to administratively close the protocol for non-compliance. A continuing review submission guide can be found on the Clinical Investigation Department (CID) SharePoint (https://esportal.med.navy.mil/nmcp/dir/dpe/ci/Pages/EIRB.aspx).

b. Modifications. Future modifications (including, but not limited to, changes in study personnel, inclusion/exclusion criteria, subject enrollment, or study procedures) must be submitted for IRB review and approval prior to implementation. If scheduled for Temporary Duty (TDY/TAD) of **4 weeks or greater**, Permanent Change of Station (PCS), or Expiration of Time in Service (ETS), the PI must request a change of PI or research study closure and give the research study files to the new NMCP PI or the

Department Chief/Head to fulfill research study completion or records retention requirements. A modification submission guide can be found on the CID SharePoint (https://esportal.med.navy.mil/nmcp/dir/dpe/ci/Pages/EIRB.aspx).

c. Event Reporting. Any deviation to the protocol that may affect the safety or rights to study subjects or the integrity of the study, Unanticipated Problems Involving Risk to Subjects or Others (UPIRTSOs), and all Serious Adverse Events (SAEs) must be promptly reported to the IRB and local HRPP via telephone (757) 953-5939 or via email (usn.hampton-roads.navhospporsva.list.nmcp-irboffice@health.mil) within ONE business day of discovery. A Reportable Event form must be submitted within THREE business days of discovery. An Adverse Event (AE) that is neither serious, nor unexpected, nor related to research, should be reported to the IRB and local HRPP at the time of continuing review. If investigators are unsure of the classification of an event, they should contact the IRB or local HRPP. A Reportable Event submission guide can be found on the CID SharePoint (https://esportal.med.navy.mil/nmcp/dir/dpe/ci/Pages/EIRB.aspx).

d. Closure. When the project has been completed, a Closure Report and a manuscript, abstract, or summary of study results must be submitted. If research cannot be completed, a Closure Report must be submitted along with an explanation of why the project will not continue. It is the PI's responsibility to ensure that Closure Reports are uploaded to DTIC (https://discover.dtic.mil) within 90 days of closure. A DTIC submission guide can be found on the CID SharePoint https://esportal.med.navy.mil/nmcp/dir/dpe/ci/Pages/IRB Submission Guidance.aspx).

8. Publication. All abstracts, presentations, manuscripts, and review articles must be approved by the local command prior to submission for publication. At NMCP, approval request forms may be obtained from the CID SharePoint (https://esportal.med.navy.mil/nmcp/dir/dpe/ci/Pages/Publication Approval.aspx). Investigators from other commands should contact their local Public Affairs Office.

9. Funding. Approval of this study does not guarantee that funds are available to support it. If funding for supplies, equipment, or personnel is required, contact the NMCP Directorate of Professional Education or the PI's local command.

10. Contacts. The local HRPP contact at Naval Medical Center Camp Lejeune is Ms. Chemely Walker (chemely.m.walker.civ@health.mil, (910) 450-3460).

The NMCP IRB Office may be contacted at (757) 953-5939 or via email at usn.hampton-roads.navhospporsva.list.nmcp-irboffice@health.mil. SOPs, policies, and guidance can be found on the CID SharePoint (https://esportal.med.navy.mil/nmcp/dir/dpe/ci/).

Kersten Wheeler

Signature applied by Kersten N Wheeler on 04/28/2025 02:22:27 PM CDT

NMCP IRB OFFICE

# EIRB Protocol Template (Version 1.5)

## 1.0 General Information

***Please enter the full title of your protocol:**

A single-center, patient- and assessor-blinded, randomized controlled trial to compare patient outcomes between Deflated and Inflated Cuff Endotracheal Extubations proceeding scheduled, non-airway surgery in healthy adults (DICEE)

***Please enter the Protocol Number you would like to use to reference the protocol:**

DICEE
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this protocol.

**Is this a multi-site protocol (i.e. Each site has their own Principal Investigator)?**

No

**Does this protocol involve the use of animals?**

○ Yes ◉ No

## 2.0 Add departments

**2.1 List sites associated with this study:**

| Is Primary? | Site Name |
|---|---|
| ◆ | **P and R** - Naval Medical Center Camp Lejeune (NMCCL) |

## 3.0 ■ Assign project personnel access to the project

**3.1 * Please add a Principal Investigator for the study:**

| Name | Role | Training Record |
|---|---|---|
| **Lee, Michael A** | **Principal Investigator** | **View Training Record** |

Responsibility

☐ Student
☐ Resident
☐ Site Chair
☐ Fellow

**3.2 If applicable, please select the Research Staff personnel:**

A) Additional Investigators

| Name | Role | Training Record |
|---|---|---|
| HICKS, Leslee Lynne, Speech-language pathology | Associate Investigator | View Training Record |
| Rodriguez, Gabriel A | Associate Investigator | View Training Record |
| Schmidt, Rolf | Associate Investigator | View Training Record |
| Willett, Peter Bryce | Associate Investigator | View Training Record |

B) Research Support Staff

| Name | Role | Training Record |
|---|---|---|
| Adams, Ashley R | Statistician | View Training Record |
| Chalas-Reid, Kathiusca Arielis | Research Coordinator | View Training Record |
| Kelly, Shannon Yvette, BS Clinical Research | Research Coordinator | View Training Record |

**3.3 *Please add a Protocol Contact:**

| Name | Role | Training Record |
|---|---|---|
| Chalas-Reid, Kathiusca Arielis | Study Contact | View Training Record |
| Kelly, Shannon Yvette, BS Clinical Research | Study Contact | View Training Record |
| Lee, Michael A | Study Contact | View Training Record |

The Protocol Contact(s) will receive all important system notifications along with the Principal Investigator. (i.e. The protocol contact(s) are typically either the Protocol Coordinator or the Principal Investigator themselves).

**3.4 If applicable, please select the Designated Site Approval(s):**

| Name | Role | Training Record |
|---|---|---|
| No Designated Department Approval have been added | | |

Add the name of the individual authorized to approve and sign off on this protocol from your Site (e.g. the Site Chair).

## 4.0 Project Information

**4.1 * What department(s) will be associated with this protocol?**

| | |
|---|---|
| | Anesthesiology |

**4.2 * Is the IRB of record for this study an IRB/HRPP that does NOT use EIRB? If Yes, complete the application according to the IRB/HRPP Determination.**

**If your Projects or Protocols are under the oversight of another IRB that does use EIRB, stop this submission and contact the core site and request an invitation as a performing site.**

**If your Project or Protocol is now being submitted for the first time to an IRB that does use EIRB, continue with this application and answer the questions to be reviewed by the IRB.**

Answering yes means the board of record is an IRB that does NOT use EIRB.

○ Yes ◉ No

**4.3 * Is this protocol research, expanded access, or humanitarian use device?**

◉ Yes ○ No

**4.4 * What type of protocol is this?**

- ☐ Behavioral Research
- ☐ Biomedical Research
- ☑ Clinical trial (FDA regulated)
- ☐ Educational Research
- ☐ Expanded Access
- ☐ Humanitarian Use Device (HUD)
- ☐ Psychosocial Research
- ☐ Oral History
- ☐ Other

**4.5 Are you conducting this project in pursuit of a personal degree?**

○ Yes ◉ No

**4.7 * Is this human subjects research? (As defined by 32 CFR 219) Human subject means a living individual about whom an investigator (whether professional or student) conducting research:**
**(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or**
**(ii) Obtains, uses, studies, analyzes or generates identifiable private information or identifiable biospecimens.**

◉ Yes ○ No

**4.8 * Do you believe this human subjects research is exempt from IRB review?**

○ Yes ◉ No

## 5.0 Personnel Details

**5.1 Does the Principal Investigator have a Permanent Change of Station (PCS) Date or Estimated Institutional Departure Date (EIDD)?**

○ Yes ◉ No

**5.2 List any Research Team members without EIRB access that are not previously entered in the protocol:**

No results found

**5.3 Are any Contractors or Subcontractors involved in this study? If yes, please list them and describe their role.**

(•) Yes ( ) No

| | | | |
|---|---|---|---|
| Name: (Last, First, M.I.)<br>Adams, Ashley R<br>Role on Protocol:<br>Statistician | Phone Number:<br>910-449-2862 | Email Address:<br>ashley.r.adams29.ctr@health.mil | Associated Institution:<br>NMCCL |
| Name: (Last, First, M.I.)<br>Kelly, Shannon Y<br>Role on Protocol:<br>Research Coordinator | Phone Number:<br>910-450-3437 | Email Address:<br>shannon.y.kelly.ctr@health.mil | Associated Institution:<br>NMCCL |
| Name: (Last, First, M.I.)<br>Chalas-Reid, Kathy A<br>Role on Protocol:<br>Research Coordinator | Phone Number:<br>910-450-5082 | Email Address:<br>kathiusca.a.chalas-reid.ctr@health.mil | Associated Institution:<br>NMCCL |

**5.4 Will you have a Research Monitor for this study?**

(•) Yes
( ) No
( ) N/A

**Research Monitor Qualifications**
Ensure the individual has expertise consistent with the nature of risk(s) identified within your study and is independent of the team conducting the research.

Research Monitor Role:

The Data Monitor will be responsible for reviewing severe adverse events that require specialty consults, spot checking data entry for accuracy, and confirming that study protocols are being followed.

If applicable, you may nominate an individual to serve as the Research Monitor:

| Selected Users |
| --- |
| Devon Nicole KOVACS |

## 6.0 Data/Specimens

**6.1 Does the study involve the use of existing data or specimens only (no interaction with human subjects)?**

○ Yes ◉ No

## 7.0 Funding and Disclosures

**7.1 Source of Funding:**

| Funding Source | Funding Type | Amount |
| --- | --- | --- |
| No results found | | |

Total amount of funding:

0

**7.2 Do you or any other Investigator(s) have a disclosure of a personal interest or financial nature significant with sponsor(s), product(s), instrument(s) and/or company(ies) involved in this study?**

○ Yes ◉ No

All personnel engaged in research must complete and attach a Conflict of Interest (COI) form.

## 8.0 Study Locations

**8.1 Is this a collaborative or multi-site study? (e.g., are there any other institutions involved?)**

○ Yes ◉ No

**8.2 Study Facilities and Locations:**

| Institution | Site Name | Site Role | FWA or DoD Assurance Number | Assurance Expiration Date | Is there an agreement? | IRB Reviewing for Site |
| --- | --- | --- | --- | --- | --- | --- |
| Navy | Naval Medical Center | Performance | | | | : Other |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Camp Lejeune | site | | | | |

Other:

| Other Institution Site | Site Role | FWA or DoD Assurance Number | FWA or DoD Expiration Date | Is there an agreement? | IRB Reviewing for Site |
|---|---|---|---|---|---|
| No results found | | | | | |

**8.3 Are there international sites?**

Attach international approval documents, if applicable, when prompted. Note: Ensure local research context has been considered

○ Yes ◉ No

**8.4 Is this an OCONUS (Outside Continental United States) study?**

○ Yes ◉ No

Select the area of responsibility:

Have you obtained permission from that area of responsibility? (This is a requirement prior to study approval)

○ Yes ○ No

## 9.0 Study Details

**9.1 Key Words:**

Provide up to 5 key words that identify the broad topic(s) of your study

Randomized Controlled Trial
Deflated Cuff Extubation
Inflated Cuff Extubation
Airway Contamination
Patient Outcomes

**9.2 Background and Significance:**

Include a literature review that describes in detail the rationale for conducting the study. Include descriptions of any preliminary studies and findings that led to the development of the protocol. The background section should clearly support the choice of study variables and explain the basis for the research questions and/or study hypotheses. This section establishes the relevance of the study and explains the applicability of its findings

The current standard anesthetic practice for extubation is to deflate the endotracheal tube cuff using a syringe prior to extubation [1]. While commonplace and nearly universally accepted, this practice is not based on evidence from randomized controlled trials [2] but is instead due to concern for laryngeal or vocal cord injury and arytenoid cartilage dislocation [3]. However, no publications exist in the medical literature that attribute laryngeal trauma directly to inflated cuff endotracheal tube extubation, as opposed to the process of extubation in general [4]. To the contrary, case reports that describe peri-operative extubation with unintentionally inflated cuffs all note the absence of negative outcome [5, 6].

Alternatively, extubation with an inflated endotracheal tube cuff has been advocated as a technique to reduce airway complications in human and veterinary medicine [1, 7, 8, 9] . Tracheal aspiration, even micro-aspiration by oropharyngeal secretions, may increase the risk of pneumonia and other pulmonary complications [10]. Based on an animal model, inflated cuff extubation may reduce airway contamination by oropharyngeal fluid [101. Additionally, leaving the endotracheal tube cuff inflated may effectively generate a vital capacity breath during extubation, maximizing oxygen reserves and facilitating a secretion-clearing cough [12]. These theorized advantages may prolong the time to which supplemental oxygen is required as well as decrease airway/respiratory complications in the immediate post-extubation period.

Within the intensive care setting, unplanned extubation (including accidental extubation and self-extubation) occurs at a rate of 3% to 16% of intubated patients or 0.1 to 3.6 per 100 days of mechanical ventilation [13, 14, 15, 16]. Estimates of national hospitalizations requiring mechanical ventilation approach 800,000, thereby placing the estimated number of unplanned extubations between 24,000 and 128,000 [17]. Presumably, the majority of these unplanned extubations are with inflated cuffs, and yet still no epidemic of laryngeal trauma from inflated cuff extubation exists. Furthermore, there have been no significant differences in laryngeal complications reported between planned and unplanned extubation in the intensive care population, suggesting that it is the endotracheal tube itself (and the process of placing it) that confers the risk of laryngeal complications, rather than the circumstances of its removal [18, 19].

Though several providers have published their success with inflated cuff extubation, to date no prospective, randomized controlled trial has been performed directly comparing these two techniques. We propose to study the effect of inflated cuff extubation on airway contamination by oropharyngeal material, extubation quality, post-extubation oxygenation, and laryngeal symptoms compared to the standard technique of deflated cuff extubation.

To assess the difference in aspiration rates between deflated and inflated cuff extubation, we propose to use radio-opaque contrast material introduced into the oropharynx of intubated patients while under general anesthesia. Two prior studies have instilled contrast media into the oropharynx of intubated patients while under general anesthesia to evaluate incidence and severity of pulmonary contamination [20, 21], demonstrating aspiration in 75% and 20% of patients, respectively. These studies compared different methodologies of removing gastric contents and oropharyngeal contents. The aspiration rates of conventional secretion-clearing techniques in these studies were 100% and 30%, respectively. A study evaluating continuous suction of subglottic secretions demonstrated a lower-airway contamination rate of 56% in the control group that reflected conventional practice [22]. Although this study used fiberoptic bronchoscopy and methylene blue, we hold that its protocol most accurately resembles modern technique and equipment, as well as the aims of our study. Of note, a related study used 15 ml of barium sulfate introduced into the oropharynx of patients under general anesthesia to demonstrate the protection from aspiration conferred by an endotracheal tube or laryngeal mask airway [23]. However, no post-extubation films were taken. These authors did opine that radiographic exams for aspirated contrast material would be more sensitive that fiberoptic examination for methylene blue.

Careful consideration went into selecting our contrast agent, as the medium needed to be adequately sensitive to detect aspiration on plain film x-ray and, importantly, to present minimum risk to research subjects. Barium sulfate is a widely used contrast agent often used for swallow studies in which aspiration is possible. While some patient may tolerate low volume barium aspiration without symptoms, severe respiratory distress and even mortality has been reported [24]. In patients at risk for aspiration, low-osmolar water-soluble contrast agents such as iohexol (omnipaque) have been advocated as safer alternatives that barium and high-osmolar water-soluble contrasts agents [25, 26, 27, 28]. Two large studies encompassing a total of 2,733 exams compared iohexol to barium to assess its suitability for swallow study [29, 30]. Harris et al identified 36 aspiration events with iohexol, noting that 4-5 ml of iohexol (omnipaque 350) was initially given "when aspiration was of concern" and that the amount of aspirated iohexol was "usually less than 1ml." Harris et al also stated that the only subjects who experienced mild symptoms of pulmonary edema were three patients with fistulous connections to the airway. Only one patient, again a patient with an esophageal-airway fistula, experienced respiratory symptoms in the form of brief stridor. Hwang et al observed 147 aspiration events with iohexol (omnipaque 350) with a mean aspirated volume of 6.7 ml. Most relevant to our proposed study, Hwang et al concluded that WSCA (iohexol)-based swallowing study "was significantly better at detecting aspiration than MBSS (modified barium swallowing study)" and that "aspirated WSCS (water-soluble contrast solution) was not accompanied by significant pulmonary edema, whereas chemical pneumonitis resulted from aspirated barium.

The safety profile of intrapulmonary iohexol can also be supported by its use in tracheobronchography. Tracheobronchography is a radiologic technique in which a contrast agent is intentionally placed into the airway and then visualized by plain film x-rays, allowing examination of the tracheal and bronchial anatomy. Iohexol has been used for

tracheobronchography for neonatal, pediatric, and adult patients [31, 32, 33, 34], under general endotracheal anesthesia and sedation. Some pediatric patients were critically ill and ventilator /oxygen dependent at the time of the examination. In the case series of four adults undergoing tracheobronchography, 20-30 ml of iohexol was injected into the tracheobronchial tree. These case series all emphasize that no deteriorations in respiratory status were observed. One accidental bronchography was obtained during the conduct of an iohexol-based swallow study in which 10 ml of iohexol was aspirated [35]. That patient experienced no respiratory distress and required no supplemental oxygen administration.

**9.3 Objectives/Specific Aims/Research Questions:**

Describe the purpose and objective(s) of the study, specific aims, and/or research questions /hypotheses

The objective of this study is to compare patient outcomes between endotracheal tube inflated cuff extubation (ICE) and the conventional practice of deflated cuff extubation (DCE).

**AIM 1: Airway Contamination**
To determine the difference of lower airway contamination by pharyngeal fluid between ICE and DCE, as measured by the propagation of contrast material to or below the level of the carina, assessed by plain film radiographs.

**AIM 2: Respiratory Complications**
To determine the extubation quality difference between ICE and DCE, as measured by complications of coughing, hypoxemia, airway obstruction, bronchospasm, stridor, laryngospasm, and aspiration.

**AIM 3: Supplemental Oxygen**
To determine the difference in post-extubation oxygenation between ICE and DCE, as measured by the need for and time to supplemental oxygen administration.

**AIM 4: Laryngeal Complications**
To determine the relative risk of laryngeal complications between ICE and DCE, as measured by symptoms of hoarseness, dysphonia, sore throat, cough, and dysphagia 24 to 48 hours postoperatively.

**9.4 Study Design:**

Describe study design in one to two sentences (e.g., prospective, use of existing records/data /specimens, observational, cross-sectional, interventional, randomized, placebo-controlled, cohort, etc.). Specify the phase – Phase I, II, III, or IV – for FDA-regulated investigational drug research

This is a single-center, patient- and assessor-blinded, parallel arm, prospective, interventional, randomized controlled trial.

**9.5 Target Population:**

Describe the population to whom the study findings will be generalized

Healthy adult patients undergoing scheduled, non-airway surgeries

### 9.6 Benefit to the DoD:

State how this study will impact or be of benefit to the Department of Defense

This study will be the first to evaluate the inflated cuff extubation technique. It has published support by practicing anesthesiologists and potential advantages supported by an animal model study. Refinement of peri-operative extubation practices may result in fewer airway or respiratory complications, improving patient safety and experience.

## 10.0 Study Procedures, Data Management, and Privacy

### 10.1 Study Procedures:

Describe step-by-step how the study will be conducted from beginning to end

**Standard of Care Intubation and Airway Management (ALL PATIENTS)**
All patients will be intubated using standard of care procedures at NMCCL.
Induction of anesthesia will involve the use of neuromuscular blocking agents to facilitate laryngoscopy. Otherwise, induction of anesthesia will be at the discretion of the PI.
Oropharyngeal and/or nasopharyngeal airways will be placed only if deemed necessary to adequately mask ventilate. Intubation will be performed by the PI via direct laryngoscopy only. Biologic males will be intubated with a 7.5mm internal diameter 10.2 outer diameter Sheridan /HVT endotracheal tube, product reference number 5-10315, with the cuff placed approximately 3-4 cm distal to the vocal cords. Biologic females will be intubated with a 7.0mm internal diameter, 9.6mm external diameter Sheridan/HVT endotracheal tube, product reference number 5-10314, with the cuff placed approximately 3-4 cm distal to the vocal cord. No local anesthetics will be topically applied to the airway or the endotracheal tube. Following endotracheal intubation, the endotracheal tube will be secured with adhesive tape and the cuff pressure will be confirmed to be in the range of 25-30 cm H2O.
All patients will receive dexamethasone 0.2mg/kg IV within thirty minutes of intubation. No nitrous oxide will be administered. Patients will otherwise be administered an anesthetic maintenance plan deemed most suitable based on their clinical circumstances and the surgical intervention, per the judgment of the PI. Use of orogastric tube will be noted. Ventilation will be performed with tidal volumes 5-7 ml/kg ideal body weight, fractional inspiratory concentration of oxygen between 21-50%, positive end-expiratory pressure 5-15 cm H2O, and a respiratory rate titrated to an end-tidal carbon dioxide concentration of 35-40 mmHg.

**Extubation (ALL PATIENTS)**
Approximately 20 minutes prior to end-of-surgery, a nasal cannula with end-tidal carbon dioxide sampling capability will be appropriately positioned on the patient. The endotracheal tube cuff pressure will be re-checked to confirm it is within a range of 25-30 cm H2O. Any indwelling gastric tube will be removed without applying suction to the oropharynx. The patient will be returned to a leveled position.
To identify the presence of airway contamination in the post-operative x-ray, 20 ml of the contrast material iohexol 350 (Omnipaque) will be instilled into the oropharynx via syringe. This procedure is for research purposes only and is not standard of care. A soft bite block will be placed. At end-of-surgery, the fractional inspiratory concentration of oxygen will be increased to 100% with fresh gas flow at 10 liters/min. Oropharyngeal contents will be removed blindly with a rigid Yankauer suction catheter. Sugammadex 2-4mg/kg for reversal of neuromuscular blockade will be administered. A regular breathing pattern and adequate spontaneous ventilation will be established. Continuous positive airway pressure will be set to 10 cm H2O.

**Allocation (ALL PATIENTS)**
The PI will then open the sealed envelope corresponding to the patient's Study ID to reveal the patient's group allocation. On eye-opening and/or purposeful spontaneous movement, the principal investigator will then perform either Deflated Cuff Extubation (DCE) or Inflated Cuff Extubation (ICE) as assigned. An Anesthesiologist AI will be present in the OR to collect research data but will be blinded to the patient's allocation.

**Arm 1 – Deflated Cuff Extubation**
The adjustable pressure-limiting (APL) valve will be set to 20 cm H2O. All air will be removed from the endotracheal tube cuff pilot balloon with a 10ml syringe. The endotracheal tube will be withdrawn into an opaque blue towel, to prevent the Anesthesiologist AI from identifying the

patient's allocation, while the reservoir bag is simultaneously compressed to generate at least 20 cm H2O positive airway pressure.

**Arm 2 – Inflated Cuff Extubation**
The APL valve will be set to 20 cm H2O. To blind the Anesthesiologist AI from the patient's group allocation, sham deflation of the endotracheal tube cuff pilot balloon will be performed with a 10ml syringe. The endotracheal tube will be withdrawn into an opaque blue towel while the reservoir bag is simultaneously compressed to generate at least 20 cm H2O positive airway pressure. In the rare event significant resistance is met with attempted extubation, the principal investigator will deflate the cuff in one milliliter increments until extubation is possible. This process does not unblind the Anesthesiologist AI.

**Post-Extubation (ALL PATIENTS)**
The PI will confirm positive end-expiratory carbon dioxide via the anesthesia mask and circuit. Once airway patency is confirmed, supplemental oxygen will be withdrawn. Ventilation will be monitored by nasal cannula end-tidal carbon dioxide sampling.
When supplemental oxygen is withdrawn, the Anesthesiologist AI will then begin a six-minute timer, during which time any airway complications, further supplemental oxygenation via the nasal cannula (as determined by if the patient's arterial oxygenation reaches 94% or lower by pulse oximetry), or other interventions performed will be recorded, along with the time elapsed, in the medical record and on the research data collection tool (DCT).
As is standard, following the observation period the patient will be transferred to the Post-Anesthesia Care Unit (PACU) in the semi-upright position if medically able.
To answer the primary research question of airway contamination, the patient will receive a portable anteroposterior chest x-ray in the semi-upright position in Phase 1 recovery. The x-ray order will be placed by the PI. If a delay occurs, the chest x-ray can be taken in Phase 2 recovery. If the portable chest x-ray is not available, the chest x-ray will be obtained in the radiology department.
An investigator will confirm the patient's ability to phonate before discharge from Phase 1 recovery. Otolaryngology will be urgently consulted in the event the patient does not recover ability to phonate or if symptoms consistent with critical upper airway obstruction develop, as is the NMCCL policy.
After the patient has been discharged from the PACU, the Anesthesiologist AI will collect demographic and comorbidity data from the patient chart to add to the research DCT. The patient will receive a one-page symptom diary on which to record answers regarding their potential laryngeal complications for the first 24 hours, to aid them in recalling their symptom details for the post-op phone call.

**Post-Operative Day 1-2 (ALL PATIENTS)**
24 to 48 hours postoperatively, the SLP AI will contact the patient. Most participants are expected to have already been discharged at this point. For these participants, the SLP AI will contact them by phone, using the postoperative telephone script. For participants still in the hospital, the SLP AI will visit the participant's patient room. The SLP AI will assess for the following: sore throat presence/severity, cough symptom score, voice quality (as measured by Grade, Roughness, Breathiness, Asthenia and Strain, also known as the GRBAS scale), and dysphagia presence/severity. This data will be recorded on a research DCT. Patients will be then informed that their participation in the research study is complete.
If the SLP AI is not available, this phone call or room visit will be made by a member of the study staff who is not the PI and the data will be provided to the SLP AI. Further evaluation for laryngeal dysfunction will be at the professional judgment of the SLP AI. Any evaluation beyond the data collected in the phone call will not be included in the research data.
Three attempts will be made by study staff to contact the patient via telephone. Participants who are not able to be contacted by phone will be considered lost to follow up.

**10.2 Data Collection:**

Describe all the data variables, information to be collected, the source of the data, and how the data will be operationally measured.

## Primary Outcome: Airway Contamination

Airway contamination will be measured by the presence of contrast in the airway following the extubation. After the endotracheal tube has been inflated, but prior to extubation, 10 ml of the contrast material iohexol will be instilled into the patient's oropharynx. This contrast material will serve as a radio-opaque marker to assess on plain film x-rays whether oropharyngeal secretions have entered the airway.

To detect the presence of contrast in the airway, an anterior-posterior (AP) chest x-ray will be taken in the PACU. The presence of contrast at or below the level of the carina will be assessed by a hospital staff radiologist and will be reported as a yes or no event.

## Secondary Outcome: Laryngeal Complications

### Phonation (PACU)

After admission to the PACU but prior to PACU discharge, the patient's ability to phonate will be assessed by an AI and recorded as a yes or no event.

### Sore Throat (Postoperative)

24 to 48 hours postoperatively, the patient will be contacted by the SLP AI (or secondarily by an anesthesiologist AI) to assess sore throat. Patients will be asked to rate their sore throat over the first 24 hours postoperatively on the following 4-point Likert scale:

| Score | Description |
|---|---|
| **0** | No sore throat at any time since the operation |
| **1** | Minimal sore throat |
| **2** | Moderate sore throat |
| **3** | Severe sore throat |

Sore throat will be reported both as a yes or no event and also by severity level.

### Cough (Postoperative)

24 to 48 hours postoperatively, the patient will be contacted by the SLP AI (or secondarily by an anesthesiologist AI) to assess cough. Patients will be asked to rate their cough over the first 24 hours postoperatively using the Simplified Cough Score (SCS) [36, 37] for both the daytime and nighttime.

### Voice Quality (Postoperative)

24 to 48 hours postoperatively, the patient will be contacted by the SLP AI (or secondarily by an anesthesiologist AI) to assess their voice quality. The AI will rate the patient's voice quality using the Grade, Roughness, Breathiness, Aesthenia and Strain (GRBAS) scale [38, 39].

### Dysphagia (Postoperative)

24 to 48 hours postoperatively, the patient will be contacted by the SLP AI (or secondarily by an anesthesiologist AI) to assess dysphagia. Patients will be asked to rate their difficulty swallowing over the first 24 hours postoperatively using the Bazaz Dysphagia Score (BDS). [40]

## Secondary Outcome: Respiratory Complications

Post-extubation respiratory complications include coughing, hypoxemia, airway obstruction, bronchospasm, stridor, laryngospasm, and aspiration. These complications will be measured for six minutes following the confirmation of airway patency and withdrawal of supplemental oxygen.

### Cough

Post-extubation cough severity will be determined by the Modified Minogue Scale, or MMS [41, 42]. The most severe grade that occurs during the six-minute window will be recorded on the DCT.

### Hypoxemia

Hypoxemia will be measured by any pulse oximetry reading with an appropriate plethysmographic waveform. It will be reported both as a yes or no event and also by severity level during the six-minute window. Hypoxemia levels will be defined as follows:

| Hypoxemia Level | Description |
|---|---|
| **None** | $Spo_2 \geq 95\%$ |
| **Mild** | $Spo_2$ 91% - 94% |
| **Moderate** | $Spo_2$ 86% - 90% |
| **Severe** | $Spo_2$ 80% - 85% |
| **Critical** | $Spo_2 \leq 79\%$ |

The most severe level that occurs during the six-minute window will be recorded on the DCT.

### Obstruction

Obstruction will be defined as the narrowing or occlusion of the airway by supraglottic anatomical structures resulting in impaired ventilation and will be recorded as a yes or no event during the six-minute window.

### Stridor

Stridor will be defined as an abnormal, high-pitched respiratory sound produced by irregular airflow in a narrowed airway and will be recorded as a yes or no event during the six-minute window.

### Laryngospasm

Laryngospasm will be defined as partial or complete airway structure due to maladaptive reflect closure of the vocal cords and will be recorded as a yes or no event during the six-minute window.

### Aspiration

Aspiration will be defined as respiratory distress due to inhaled gastric contents as established by witnessed event, radiologic study, or bronchoscopy. It will be recorded as a yes or no event during the six-minute window.

### Bronchospasm

Bronchospasm will be defined as deleterious spasmodic bronchial smooth muscle contraction and will be recorded as a yes or no event during the six-minute window.

## Secondary Outcome: Supplemental Oxygen

Should a patient's arterial oxygenation reach 94% or lower after extubation, the patient will be supplied with supplemental oxygen. If this occurs, the need for supplemental oxygen will be recorded as a yes or no event, as will the time in minutes at which this event occurs.

# List of Variables:

| Variable | Timing | Measurement | Type |
|---|---|---|---|
| **Age** | DOS Pre-Op | Years | Numeric |
| **Biological Sex** | DOS Pre-Op | M/F | Categorical |
| **Weight** | DOS Pre-Op | kg | Numeric |
| **Height** | DOS Pre-Op | cm | Numeric |
| **ASA Status** | DOS Pre-Op | 1,2,3 | Ordinal |
| **GERD** | DOS Pre-Op | Y/N | Categorical |
| **Asthma** | DOS Pre-Op | Y/N | Categorical |
| **Smoking** | DOS Pre-Op | Y/N | Categorical |
| **Other Significant Comorbidities** | DOS Pre-Op | Text | Categorical |
| **Pre-Operative $SpO_2$** | DOS Pre-Op | % | Numeric |
| **Pre-Operative Voice Quality** | DOS Pre-Op | Grade, Roughness, Breathiness, Aesthenia and Strain (GRBAS) scale | Ordinal |
| **Date Of Surgery** | DOS Pre-Op | DDMMMYYYY | Date /Time |
| **Indication Of Surgery** | DOS Pre-Op | Text | Categorical |

| | | | |
|---|---|---|---|
| **Start Of Surgery Time** | DOS Intubation | 2400 Format | Date /Time |
| **Time Of Intubation** | DOS Intubation | 2400 Format | Date /Time |
| **Completed Procedure** | DOS Intubation | Y/N | Categorical |
| **End Of Surgery Time** | DOS Intubation | 2400 Format | Date /Time |
| **Maintenance Medications** | DOS Intubation | Text | Categorical |
| **Emergence Medications** | DOS Intubation | Text | Categorical |
| **Contrast Instillation Time**<br>**Extubation Time** | DOS Extubation<br>DOS Extubation | 2400 Format<br>2400 Format | Date /Time<br>Date /Time |
| **Out Of Room Time** | DOS Extubation | 2400 Format | Date /Time |
| **$SpO_2$ At Extubation** | DOS Extubation | % | Numeric |
| **Cough** | DOS Extubation | Modified Minogue Scale | Ordinal |
| **Laryngospasm** | DOS Extubation | Y/N | Categorical |
| **Obstruction** | DOS Extubation | Y/N | Categorical |
| **Bronchospasm** | DOS Extubation | Y/N | Categorical |
| **Stridor** | DOS Extubation | Y/N | Categorical |
| **Additional Suctioning** | DOS Extubation | Y/N | Categorical |
| **Chin Lift** | DOS Extubation | Y/N | Categorical |
| **Positive Pressure** | DOS Extubation | Y/N | Categorical |
| **2-Hand Jaw Thrust** | DOS Extubation | Y/N | Categorical |
| **Oral Airway** | DOS Extubation | Y/N | Categorical |
| **Medications Needed** | DOS Extubation | Y/N | Categorical |
| **Type of Medication Used** | DOS Extubation | Text | Categorical |
| **Time To Supplemental Oxygen** | DOS Extubation | Seconds | Numeric |
| **Oxygen Source** | DOS Extubation | Room Air, Nasal Cannula, Simple Face Mask, Anesthesia Circuit | Categorical |
| **$O_2$ Flow** | DOS Extubation | L/min | Numerical |
| **$SpO_2$ At 6Mins Post-Extubation** | DOS Extubation | % | Numerical |
| **PACU Arrival Time** | DOS PACU | 2400 Format | Date /Time |
| **Ability To Phonate** | | Y/N | |

| | | | |
|---|---|---|---|
| | DOS PACU | | Categorical |
| **Airway/Respiratory Complications** | DOS PACU | Y/N | Categorical |
| **Description of Complication** | DOS PACU | Text | Categorical |
| **Presence of Contrast on X-Ray** | DOS PACU | Y/N | Categorical |
| **PACU Discharge Time** | DOS PACU | 2400 Format | Date /Time |
| **Sore Throat** | 24 hours postoperative | 4-pt Likert Scale, 0-3 | Ordinal |
| **Cough** | 24 hours postoperative | Simplified Cough Score | Ordinal |
| **Voice Quality** | Postoperative<br>24 hours postoperative | Grade, Roughness, Breathiness, Aesthenia and Strain (GRBAS) scale | Ordinal |
| **Dysphagia** | 24 hours postoperative | Bazaz Dysphagia Score | Ordinal |

## *Symptom Assessment Scales*

### *Modified Minogue Scale (MMS)*

Post-extubation cough severity will be determined by the Modified Minogue Scale, or MMS. The MMS is a 5-point scale, where a patient's cough is graded from 1 to 5. [41, 42] Higher grades are associated with more severe coughing, as seen below. The MMS is an assessment of coughing after emergence from general anesthesia and modifies 3-point and 4-point cough scales that had been used previously, [41, 42] having been adjusted to improve validity of the scale. There is currently no reliability data from this scale.

| Grade | Description |
|---|---|
| **1** | No coughing or muscular stiffness |
| **2** | Transient cough response to the removal of the tracheal tube that resolves after extubation |
| **3** | Moderate coughing (# 3 coughs, each lasting for 1-2 seconds |
| **4** | Severe cough or muscular stiffness (# 4 coughs, each lasting > 2 seconds) |
| **5** | Severe restlessness and associated laryngospasm |

### *Simplified Cough Scale (SCS)*

The SCS will be used to assess cough severity postoperatively. The SCS is a 2-item score for daytime and nighttime severity, rated on a 4-point scale from 0 to 3, in which a higher score indicates increased severity, as shown below. Internal consistency of the SCS is acceptable, with a Cronbach's # between 0.74 to 0.90. Additionally, the SCS's repeatability is high, with an interclass correlation coefficient of 0.76. [37]

| Score | Daytime Description | Nighttime Description |
|---|---|---|
| **0** | No cough | No cough |

| | | |
|---|---|---|
| **1** | Occasional transient cough during the day | Occasional transient cough before sleep or during the night |
| **2** | Frequent cough mildly affecting daily life | Cough mildly affecting night sleep |
| **3** | Frequent cough severely affecting daily life | Cough severely affecting night sleep |

***Grade, Roughness, Breathiness, Aesthenia, Strain (GRBAS) Scale***

The GRBAS scale will be used to assess voice quality pre- and postoperatively. On the GRBAS scale, each item on the scale is scored from 0 to 3, where 0 is normal voice quality for that item, and 3 is severely abnormal. Definitions for the voice qualities measured by GRBAS are as follows:

| Component | Description |
|---|---|
| **Grade** | Degree of hoarseness of the voice |
| **Roughness** | Impression of irregularity of the vibration of the vocal folds |
| **Breathiness** | Degree to which air escaping from between the vocal folds can be heard by the examiner |
| **Asthenia** | Degree of the weakness heard in the voice |
| **Strain** | Extent to which strain or hyperfunctional use of phonation is heard |

Test-retest reliability, intra-rater reliability and inter-rater reliability of the GRBAS scale are satisfactory. Test-retest reliability coefficients range from .75 to .83, intra-rater reliability coefficients range from .69 to .81, and inter-rater reliability coefficients range from .69 to .78, with an exception for Strain, which has a lower inter-rater reliability of .48. [43, 44]

***Bazaz Dysphagia Score (BDS)***

The BDS will be used to assess postoperative dysphagia. The BDS is a 4-point Likert scale from 0 to 3, with a larger score indicating a higher severity of dysphagia. Though no formal validity or reliability data have been established, the BDS is both the first and most popular patient-reported objective measure of dysphagia. [40, 45]

| Score | Grade | Description |
|---|---|---|
| **0** | *None* | No episodes of difficulty swallowing |
| **1** | *Mild* | Only rare episodes of difficulty swallowing |
| **2** | *Moderate* | Occasional swallowing difficulty with solid foods |
| **3** | *Severe* | Swallowing difficulty with solids and liquids |

**10.3 At any point in the study, will you request, use, or access health information in any form, including verbal, hard copy and electronic?**

(•) Yes ( ) No

**10.4 Review the definitions below and respond to the following two questions. If you are not sure of the answers, email DHA.PrivacyBoard@mail.mil for assistance. The *Military Health System (MHS)* is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force *MHS workforce members* are employees, volunteers, trainees, and other persons whose conduct, in the performance of work for the MHS, is under the direct control of the MHS, whether or not they are paid by the MHS. *MHS business associates* are persons or entities that provide a service to the MHS and require protected health information (PHI) to provide the service.**

**Are you an MHS workforce member?**

- (•) Yes, I am an MHS workforce member
- ( ) No, I am not an MHS workforce member

**10.5 Have you consulted with an MHS data expert to determine the data elements required for your study?**

Consulting with a data expert often saves time later in the compliance process because the data expert can advise on the data available in the numerous MHS information systems, the quality of that data and the methods for encrypting and collapsing data. To schedule a consult with an MHS data expert, send an email to: (**DHA.PrivacyBoard@mail.mil**)

- ( ) Yes, then complete the questions below according to the data consult
- (•) No, then complete the questions below according to the best of your knowledge

**10.6 Indicate how you will request data from the MHS. Select all that apply.**

- [ ] Talking with MHS health care providers or MHS health plans about specific research participants
- [ ] Obtaining MHS hard copy records specific to research participants
- [x] Obtaining data from an MHS information system(s)

**10.7 If you are obtaining data from an MHS information system(s), indicate whether you plan to receive a data extract or whether you plan to access an MHS information system directly to create a data set.**

A data extract is when the MHS or a contractor provides the data set directly to the researcher. When receiving a data set through data extract, the researcher may indicate whether the data elements should be provided as is, encrypted or collapsed. In contrast to a data extract, access to an information system means that the researcher may directly access an MHS information system and create a data set for the research study

- [ ] Data Extract
- [x] Access

**10.8 Do you intend to request de-identified data from the MHS in your research study?**

There are different two methods for de-identifying data pursuant to HIPAA:
1) Safe Harbor Method: Removing all of the identifiers listed in Table 1 below, provided that the researcher does not have actual knowledge that the remaining data can be used alone or in combination with other information to identify the individual who is the subject of the information
2) Statistical Method: An expert, with appropriate knowledge of and experience with generally accepted statistical and scientific principles and methods for rendering information not individually identifiable, determines that the data is not individually identifiable

( ) Yes (•) No

**10.9 Indicate the MHS information system(s) from which you will seek to obtain data**

If you do not know which system(s) contains the data elements you need, refer to the Guide for DoD Researchers on Using MHS Data or request guidance from an MHS data expert at: **DHA.PrivacyBoard@mail.mil**.

Below is a list of commonly used MHS systems. If the system from which you seek to obtain data is not listed below, list the name of the system in the "Other MHS Systems" category below
**PHI Systems:**

| MHS Information System | Requesting Data |
|---|---|
| : MHS Genesis | : No |

**PII-Only Systems:**

| MHS Information System | Requesting Data |
|---|---|
| No results found | |

**De-Identified Data & Other Systems:**

| Information System | Requesting Data |
|---|---|
| No results found | |

**10.10 Do you intend to merge or otherwise associate the requested data with data from any sources outside of the MHS, including other DoD systems that are not part of the MHS?**

- ○ Yes, will merge data
- ◉ No, will not merge data

**10.11 Indicate the data elements about research participants or relatives, employers, or household members of the research participants that you will request from MHS hard copies or from MHS information systems.**
**If you will merge data, also indicate non-MHS data elements about research participants or relatives, employers, or household members of the research participants that you will have access to in any form or medium.**

| Direct and Indirect Identifiable Data Elements | DHA Hard Copies | DHA Data Elements to be Accessed | DHA Data Elements Verbal | Extracted DHA Digital Data | Downloaded DHA Digital Data | Non-DHA Hard Copies or Digital |
|---|---|---|---|---|---|---|
| 1. Names | ☐ | ☑ | ☐ | ☐ | ☐ | ☐ |
| 2. Postal address with only town, city, state, and zip code | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 3. Postal address with all geographic subdivisions smaller than state, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| from the Bureau of Census: 1) the geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people; and 2) the initial three digits of a zip code from all such geographic units containing 20,000 or fewer people is changed to 000 | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 4. Dates including all elements (except year) directly related to an individual, including birthdate, admission date, discharge date, and date of death | ☐ | ☑ | ☐ | ☐ | ☐ | ☐ |
| 5. Ages over 89 and all elements of dates (including year) indicative of such age, unless you will only request a single category of "age 90 or older" | ☐ | ☑ | ☐ | ☐ | ☐ | ☐ |
| 6. Telephone Numbers | ☐ | ☑ | ☐ | ☐ | ☐ | ☐ |
| 7. Fax Numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

| | | | | | | |
|---|---|---|---|---|---|---|
| 8. Email Addresses | ☐ | ☑ | ☐ | ☑ | ☑ | ☐ |
| 9. Social Security Numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 10. Medical Record Numbers (MRN) (including record ID) | ☐ | ☑ | ☐ | ☐ | ☐ | ☐ |
| 11. Health Plan Beneficiary Numbers (including DEERS ID, Electronic Data Interchange Personal Identifier (EDIPI) or Number (EDIPN)) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 12. Account Numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 13. Certificate /License Numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 14. Vehicle identifiers and serial numbers, including license plate numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 15. Device identifiers and serial numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 16. Web Universal Resource Locators (URLs) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

| | | | | | | |
|---|---|---|---|---|---|---|
| 17. Internet Protocol (IP) address numbers | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 18. Biometric identifiers, including finger and voice prints | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 19. Full-face photographic images and any comparable images | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 20. Any other unique identifying number, characteristic, or code (including non-military provider IDs) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| 21. Free Text Fields | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

If you are obtaining SSNs, provide a justification as to why and explain why a substitute cannot be used.

Due to guidelines stated within DoDI 1000.30, Reduction of SSN Use within DoD, the reduction or elimination of SSN usage must occur wherever possible. If SSNs are required to complete the project, the PI must provide a justification and explanation as to why a substitution cannot be used.
For example:

- If alternatives to SSN (e.g., EDIPNs or pseudo person IDs) are sufficient in other instances, will those alternatives to SSN usage be sufficient to respond to Congressional inquiries and /or Senior DoD stakeholders inquiries?
- Are alternatives to SSN used first?
- Are those alternatives to SSN insufficient to combine data from multiple data sources? Is the issue that some individuals do not possess alternatives ID numbers and SSN is the only way to identify them?

No SSNs will be obtained.

a. Will you receive or obtain health information?

> ***Note:*** *If you indicate you are not receiving health information, the answer must be consistent with the DHA data source. For a non-health information data request, if you are a non-MHS employee or non-MHS business associate, you may not access an information system that has PHI or LDS. For both MHS and Non-MHS employees and MHS business associates, you may* ***NOT*** *include data elements in the above table on:*

*1) lines 10 or 11, 2) line 21 if the free text field comes from a PHI or LDS system, and 3) lines 12, 13, or 18 if the account numbers, certificate and license numbers, biometric data, or any other data elements are health information created or received by an MHS health care provider, health plan, or business associate in relation to the physical or mental health or condition of an individual or payment for health care.*

- (●) Yes, I will receive or obtain health information
- ( ) No, I will not receive or obtain health information

b. If no data elements were checked in the above table, is it possible that the requested DHA data is or will be identifiable because of any unique data elements, triangulation, or small cell size?

- [x] Data elements were checked in the above table, STOP HERE.

***NOTE:*** *A unique data element includes any unique features that alone are not identifiable but that could be used to identify an individual within the context of other information, such as any type of code (such as diagnosis or procedural), rank of general or admiral, gender, or race. Triangulation means using different data elements that when combined can be used to identify an individual, such as including the above lists of unique data elements in a data set. Determining whether an individual is identifiable through triangulation requires consideration of all data elements in combination. Within the military, the use of rank and/or diagnosis code, procedural codes, or any other code that changes on a predictable basis, increases the possibility of identification. Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Department of Defense Manual 6025.13, Medical Quality Assurance and Clinical Quality Management in the Military Health System MHS, provides that the threshold for de-identifying data within the MHS requires a cell size of three, but also states that the de-identification standards must meet the DoD implementation of the HIPAA Privacy Rule. Centers for Medicare and Medicaid also gives guidance on small cell size stating that no data cell less than 11 may be published or displayed. However, the Office for Civil Rights' OCR, which is the official regulatory office for the HIPAA Privacy Rule, provides that OCR does not designate a universal value for small cell size in accordance with the de-identification standard; instead, the cell size should be set at a level that is appropriate to mitigate risk of identification by the anticipated recipient of the data set. This means that a cell size of 3 or 11 may not meet the HIPAA Privacy Rule requirements if the cell size level does not appropriately mitigate risk of identification by the anticipated recipient of the data set.*

***Note: If dates are altered as a means of de-identifying the data, diagnosis and procedural codes need to be rolled-up or collapsed. If dates are provided "as time between events," the roll-up is not necessary.***

- [ ] Yes, the DHA data will become identifiable
- [ ] No, the DHA data will not become identifiable

**10.12 Do you believe it is possible for the MHS data to become identifiable because of triangulation, a small cell size, or any unique data element(s)?**

Triangulation means using different data elements that are not themselves identifiable but that when combined can be used to identify an individual. For example, triangulation would use rank and race together to determine the identity of an individual with a particular health condition.

Small cell size means that there is only a small number of eligible individuals that satisfy the category description. Guidance for acceptable cell size is available from the Centers for Medicare and Medicaid Services. For example, the rank category of four star generals with a particular diagnosis may be less than 30, so the rank category may need to be expanded to include lower ranks.

A unique data element includes any unique features that are not explicitly enumerated in the categories of data in rows 1 – 20 of the table above (in Section 10.10), but that could be used to identify an individual. Unique data elements include characteristics that are not themselves identifying, such as the rank of general or admiral, or a race or gender, but within the context of other information could be identifiable.

- ( ) Yes, I believe there is a reasonable possibility the MHS data will become identifiable
- (●) No, I believe there is no reasonable possibility the MHS data will become identifiable

**10.13 Have you completed and uploaded an appropriate HIPAA document ( i.e. HIPAA Authorization will be obtained or Waiver/alteration of HIPAA Authorization is being requested)?**

- (•) Yes
- ( ) No
- ( ) N/A

If yes, please check which one.

- [x] HIPAA Authorization
- [x] HIPAA Waiver (Full or Partial)
- [ ] Other (please provide copies when uploading Other Study Documents)

**10.14 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for this Study:**

Include in this section the plan for acquiring data (both electronic and hard copy), access during the study, data/specimen storage and length of time stored, shipment/transmission, and the plan for storage and final disposition at the conclusion of the study. Describe any data agreements in place for accessing data within and/or outside of your institution (e.g., Data Sharing Agreement, Data Use Agreement, Business Agreements, etc.)

Data will be collected through patient interaction and inquiry into the MHS records. This information will be recorded on hard copy Data Collection Tools (DCTs), which will only be identified via the Study ID number. The DCT hard copies will be kept in a locked document safes in the Anesthesia workroom or Speech Language Pathologist's office.

A master list will be created to connect PII/PHI with the study identifier. This electronic file will be maintained by the PI, who is the only unblinded member of the study staff, in a file location that is separate from research data labeled with patient Study IDs. The master list will be password protected, and saved onto a secure, firewall-enabled DOD network, accessible only to DOD employees and contractors who can provide two-factor authorization (henceforth referred to as the *NMCCL Network*).

DCTs will be scanned and saved onto the NMCCL Network. Not all staff have access to the same folders on the network due to privacy reasons, therefore when study staff without access to the folder containing the scanned DCTs need to transcribe hard copy data into a spreadsheet, the DCTs will be encrypted, then sent via the DOD Secure Access File Exchange (SAFE; https://safe.apps.mil/).

When transcribing data from the hard copies, data will be recorded in a spreadsheet in which patients are only identified by their Study ID. This file will also be stored on the NMCCL Network, although in a separate file location from the master list.

Files containing PII or PHI will be destroyed 6 years from IRB closure of the study in accordance with HIPAA regulations. The study team will work with IMD to employ hardware or software to enable sanitization or destruction of data following IMD policies and procedures of all electronic data.

Data will not be shared with any outside agencies.

All data will be de-identified prior to data analysis.

Is this a data repository?

( ) Yes (•) No

**10.15 Managing Data (Data Management and/or Sharing Plan) and/or Human Biological Specimens for Future Research:**

If the study involves collecting, storing, or banking human specimens, data, or documents (either by the Investigator or through an established repository) for FUTURE research, address. How the specimens/data will be used, where and how data/specimens will be stored (including

shipping procedures, storage plan, etc.), whether and how consent will be obtained, procedures that will fulfill subjects' request as stated in the consent, whether subjects may withdraw their data/specimens from storage, whether and how subjects may be recontacted for future research and given the option to decline, whether there will be genetic testing on the specimens, who will have access to the data/specimens, and the linkage, the length of time that data/specimens will be stored and conditions under which data/specimens will be destroyed.

N/A

Is this a data repository?

○ Yes ◉ No

## 11.0 Statistical/Data Analysis Plan

### 11.1 Data Analysis Plan and Statistical Considerations:

List the statistical methods to be used to address the primary and secondary objectives, specific aims, and/or research hypotheses. Explain how missing data and outliers will be handled in the analysis. The analysis plan should be consistent with the study objectives. Include any subgroup analyses (e.g., gender or age group). Specify statistical methods and variables for each analysis. Describe how confounding variables will be controlled in the data analysis.

Analysis will be conducted using SAS 9.4 (SAS Institute, Cary NC) or SPSS 28 (IBM Corp, Armock NY). Inferential analyses will be considered significant if the corresponding p-value is less than 0.05, and all applicable tests will be two-tailed.

Numerical variables which satisfy normality (as demonstrated by the Kolmogorov-Smirnov test) will be reported in means and standard deviations while non-normal variables will be reported in medians and interquartile ranges. All categorical variables will be reported in counts and frequencies. Effect sizes will be reported in risk ratios with 95% confidence intervals.

#### Potential Covariates

Demographics and risk factors will be compared between the DCE and ICE arms. Numerical variables will be compared using Student's t or Wilcoxon Rank Sum as appropriate. Categorical and ordinal variables will be compared with the $\chi 2$ Test of Independence, or if assumptions are not met, Fisher's Exact. In cases where multiple categories may make Fisher's Exact too cumbersome to calculate, a Monte-Carlo estimation will be used.

Demographics or risk factors for which significant differences between groups exist will be used as confounding or covariate variables in regression analyses.

#### Primary Outcome: Airway Contamination

The presence of airway contamination is a binary variable.

If there are significant demographics or risk factors, the presence of airway contamination will be analyzed using logistic regression to adjust for these covariates. Collinearity and separation of data points will be checked, and variables may be transformed (such as dummy variables for categorical variables) or combined to meet the assumptions necessary to proceed with the model. Unadjusted regressions (the effect of a single independent variable on the dependent variable) as well as an adjusted regression (the combined effects of multiple independent variables on the dependent variable) will be conducted.

If there are no significant demographics or risk factors, the presence of airway contamination will be compared between the DCE and ICE arms using the $\chi 2$ Test of Independence, or if assumptions are not met, Fisher's Exact.

#### Secondary Outcome: Laryngeal Complications

Laryngeal complications are either binary (ability to phonate, presence of sore throat) or ordinal (sore throat, post-operative cough, and voice quality).

If there are significant demographics or risk factors, laryngeal complications will be analyzed using logistic regression or ordinal logistic regression to adjust for these covariates. Collinearity

and separation of data points will be checked, and variables may be transformed (such as dummy variables for categorical variables) or combined to meet the assumptions necessary to proceed with the model. Unadjusted regressions (the effect of a single independent variable on the dependent variable) as well as an adjusted regression (the combined effects of multiple independent variables on the dependent variable) will be conducted.

If there are no significant demographics or risk factors, the ability to phonate will be compared between the DCE and ICE arms using the $\chi 2$ Test of Independence, or if assumptions are not met, Fisher's Exact. The laryngeal complications measured ordinally will be compared between the DCE and ICE arms using the Cochran-Armitage test.

### Secondary Outcome: Respiratory Complications

Respiratory complications are either binary (presence of cough, hypoxemia, obstruction, stridor or laryngospasm) or ordinal (cough severity, hypoxemia severity).

If there are significant demographics or risk factors, respiratory complications will be analyzed using logistic regression or ordinal logistic regression to adjust for these covariates. Collinearity and separation of data points will be checked, and variables may be transformed (such as dummy variables for categorical variables) or combined to meet the assumptions necessary to proceed with the model. Unadjusted regressions (the effect of a single independent variable on the dependent variable) as well as an adjusted regression (the combined effects of multiple independent variables on the dependent variable) will be conducted.

If there are no significant demographics or risk factors, the binary respiratory complications will be compared between the DCE and ICE arms using the $\chi 2$ Test of Independence, or if assumptions are not met, Fisher's Exact. The respiratory complications measured ordinally will be compared between the DCE and ICE arms using the Cochran-Armitage test.

### Secondary Outcome: Supplemental Oxygen

Supplemental oxygen was measured as either binary (need for supplemental oxygen) or numeric (time until oxygen administered).

If there are significant demographics or risk factors, the need for supplemental oxygen will be analyzed using logistic regression. Collinearity and separation of data points will be checked, and variables may be transformed (such as dummy variables for categorical variables) or combined to meet the assumptions necessary to proceed with the model. Unadjusted regressions (the effect of a single independent variable on the dependent variable) as well as an adjusted regression (the combined effects of multiple independent variables on the dependent variable) will be conducted.

If there are no significant demographics or risk factors, the need for supplemental oxygen will be compared between the DCE and ICE arms using the $\chi 2$ Test of Independence, or if assumptions are not met, Fisher's Exact.

If there are significant demographics or risk factors, the time until supplemental oxygen is administered will be analyzed using linear regression. Collinearity and separation of data points will be checked, and variables may be transformed (such as dummy variables for categorical variables) or combined to meet the assumptions necessary to proceed with the model. Unadjusted regressions (the effect of a single independent variable on the dependent variable) as well as an adjusted regression (the combined effects of multiple independent variables on the dependent variable) will be conducted.

If there are no significant demographics or risk factors, the time until supplemental oxygen is administered will be compared between the DCE and ICE arms using the Student's t-test or Wilcoxon Signed Rank, as appropriate.

**11.2 Sample Size:**

88

**11.3 Total number of subjects requested (including records and specimens):**

88

**11.4 If you are recruiting by study arm, please identify the arms of the study and how many subjects will**

**be enrolled in each arm**

Inflated Cuff Arm: 44
Deflated Cuff Arm: 44

**11.5 Please provide a justification for your sample size**

In a 2022 study of aspiration under general anesthesia, Mraovic et al [14] found that when the endotracheal tube cuff was inflated, secretions had migrated into the distal trachea in 13% of patients. Alternatively, once the cuff was deflated, 56% of patients had evidence of secretion migration. This study was small, consisting of only 50 patients, so conservate estimates were used to calculate sample size.
To detect a 30% decrease in patients experiencing aspiration (from 50% to 20%), at 80% power, where $p < .05$ is considered significant, we need 39 patients per group, for a total of 79 participants. To account for a potential 10% loss to follow up, we will need to enroll 88 total participants.

## 12.0 Participant Information

**12.1 Subject Population:**

Healthy adults aged 18 to 50 years old undergoing scheduled, non-airway surgery at Naval Medical Center Camp Lejeune.

**12.2 Age Range:**

Check all the boxes that apply. if the age range of potential subjects (specimens, records) does not match the range(s) selected, please specify in the text box.

- [ ] 0-17
- [x] 18-24
- [x] 25-34
- [x] 35-44
- [x] 45-54
- [ ] 55-64
- [ ] 65-74
- [ ] 75+

**12.3 Gender:**

- [x] Male
- [x] Female
- [ ] Other

**12.4 Special categories, check all that apply**

- [ ] Minors /Children
- [ ] Students
- [ ] Employees - Civilian
- [ ] Employees - Contractor
- [ ] Resident/trainee
- [ ] Cadets /Midshipmen
- [x] Active Duty Military Personnel

- ☐ Wounded Warriors
- ☐ Economically Disadvantaged Persons
- ☐ Educationally Disadvantaged Persons
- ☐ Physically Challenged (Physical challenges include visual and/or auditory impairment)
- ☐ Persons with Impaired Decisional Capacity
- ☐ Prisoners
- ☐ Pregnant Women, Fetuses, and Neonates
- ☐ Non-English Speakers
- ☐ International Research involving Foreign Nationals - Headquarters Review is necessary

You must also consider the requirements of DoDI 3216.02, Enclosure 3, paragraph 7.e.

**12.5 Inclusion Criteria:**

| Order Number | Criteria |
|---|---|
| 1 | Adults aged 18 to 50 years old |
| 2 | Scheduled for surgery, not of the airway, head, or neck, with anticipated case duration of less than 3 hours |
| 3 | American Society of Anesthesiologists (ASA) Physical Status Classification of 1 to 3 |

**12.6 Exclusion Criteria:**

| Order Number | Criteria |
|---|---|
| 1 | Emergent surgery, or surgery requiring prone, sitting or lateral positioning |
| 2 | Pre-existing laryngeal pathology, obstructive pulmonary disease, pulmonary hypertension, interstitial lung disease, active respiratory infection, recent pneumonia, uncontrolled asthma, or uncontrolled gastroesophageal reflux disease |
| 3 | Known difficulties with general anesthesia, such as prior anaphylactic reaction, difficult intubation or mask ventilation |
| 4 | Known allergy to iohexol or a previous severe reaction to any contrast agents |
| 5 | Unfavorable airway examination, such as Mallampati 4, limited mouth opening, and /or inability to extend neck |
| 6 | Non-compliance with ASA Practice Guidelines for Preoperative Fasting |
| 7 | Pregnancy |
| 7 | Emergent surgery, or surgery requiring prone, sitting or lateral positioning |
| 8 | Enrollment in another anesthesiology or surgery related interventional research study |
| 8 | Pregnancy |
| 11 | Surgeries scheduled on Friday or a day immediately prior to a holiday |

## 13.0 Recruitment and Consent

**13.1 Please describe the recruitment process, including how subjects will be identified and selected for the study.**

Each calendar week, the PI will examine the scheduled surgery list for upcoming procedures for which the PI is the anesthesiologist performing general endotracheal anesthesia. The PI will review the procedure scheduled to determine if the patient is a potential candidate.

Potential candidates will be contacted via telephone by the PI. The PI will make three attempts to contact the patient. If the potential candidate answers the telephone, the PI will follow a basic recruitment script approved by the IRB. It is possible the patient may ask questions outside the scope of the script and the PI will answer to the best of his clinical judgment.

If the potential candidate expresses interest in the study, they will be provided with an electronic copy of the informed consent document (ICD) via email or file transfer system of their choice. This will allow the candidate time to consider their choice to participate in the study and review the document before signing.

No voicemails or messages will be left if the patient does not answer. If recruitment is low due to unanswered phone calls, we may submit an amendment to leave a voice message or send a text.

**NMCCL.2024.L012 "Deflated vs Inflated Cuff Endotracheal Extubations"**
**RECRUITMENT TELEPHONE SCRIPT**

Good morning/afternoon/evening, this is Dr. Michael Lee calling from Naval Medical Center Camp Lejeune. May I please speak with {Patient Name}?
[PATIENT NOT AVAILABLE]
This is not an urgent matter, and {patient name} does not need to call me back. However, is there a better time for me to them call back? (*record time and date to return the call*)
[PATIENT AVAILABLE]
For your upcoming surgery, you will be receiving general anesthesia. I am reaching out to you today because you may be a candidate for a research trial that we're conducting on how general anesthesia is done. This would be completely voluntary. Would now be a good time to tell you more about this trial?
[PATIENT NOT INTERESTED]
I understand. Thank you for your time. (*hang up, note to not call again*)
[PATIENT STATES NOT A GOOD TIME]
Is there a better time I can call to tell you more? (*record time and date to return call*)
[PATIENT AVAILABLE]
Thank you. As I mentioned earlier, for your upcoming surgery, you will be receiving general endotracheal anesthesia. This means that we will drift you off asleep with anesthetic medications, and then place a breathing tube into your windpipe. We will keep you asleep and comfortable with anesthetic medications while your surgery takes place. Once the surgery is complete, we will stop giving you anesthetic medications, and you will begin to awaken from anesthesia. Before you are wide awake, we will take the breathing tube out. The process of taking out a breathing tube is called extubation. You will then go to the post-anesthetic care unit, or PACU, to recover from anesthesia and surgery.
Do you have any questions so far?
[IF YES]
(*listen to candidate's questions and answer them*)
[IF NO]
Our research concerns how we take out breathing tubes. Modern breathing tubes have a balloon-like cuff that we inflate inside your windpipe to make a seal. The cuff enables our ventilator machine to efficiently breathe for you. The cuff also keeps fluids from entering your lungs, such as your saliva and stomach juices. This cuff stays inflated during surgery.
Once surgery is over, the standard practice is to deflate the cuff and then take out the breathing tube. The reason this is standard practice is because some doctors are concerned that keeping the cuff inflated as it is taken out might harm parts of your throat, like your voice box. However, right now there haven't been any cases of inflated cuffs harming a person's throat more than a deflated cuff. We do know that when the cuff is deflated, sometimes there are cases when the remaining fluids leak into the windpipe and lungs.
Our research group wants to know if a different technique can reduce or prevent fluids from entering your lungs. We want to see if leaving the cuff inflated as we remove the breathing tube can do this.

What questions do you have before I explain the steps of the study in detail?
(*answer candidate's questions*)
If you were willing to participate in this study and are a suitable candidate, you would receive general anesthesia and undergo your scheduled surgery as planned. Towards the end of surgery, we would confirm that the breathing tube cuff was still safely inflated. We would then place a small amount of liquid contrast material in the back of your mouth. We use this contrast material so that we can find out later if any fluids entered your windpipe or lungs.
When the contrast is put in your mouth, you would still be asleep under anesthesia with the breathing tube protecting your airway. We would then remove as much of the contrast material as possible, along with all other fluids, using our normal methods.
Next, we would begin to wake you up from anesthesia. When it is safe to take the breathing tube out, we would either remove the cuff after deflating it or remove the cuff while it is still inflated. The way we remove the cuff will be selected at random.
After the breathing tube is out, we would collect information about the quality of the extubation and about how well you are breathing. Then you would be transferred to the PACU. In the PACU, we would take a chest x-ray to see if any of the contrast material moved into your windpipe or down towards your lungs.
Otherwise, you would proceed through recovery as normal. The day after your surgery, a member of the research team would call you to ask you about any symptoms you may be experiencing, like sore throat or hoarse voice. That would be the end of the research trial for you, and you would otherwise follow up with your surgeon as planned.
What questions do you have?
(*answer candidate's questions*)
Participation in this research trial is entirely optional. However, if you are willing to participate, we would like to email you a copy of our informed consent so that you may review it ahead of time. It has all the details about our study, as well as contact information if you have any more questions. You would not have to participate just because I sent you this information.
If you are willing to participate, I would meet with you before your surgery to answer any more of your questions. You would sign the informed consent document then, and that is when you would be entered into the study.
Would you be interested in having me send you more information?
[PATIENT NOT INTERESTED]
I understand. Thank you for your time. (*hang up, note to not call again*)
[PATIENT INTERESTED]
(*get contact information to send informed consent document*)
I will send you an email shortly. Feel free to discuss this study with family or friends. I look forward to answering any other questions you have after you've had a chance to read the information.
Do you have any other questions for me right now?
(*answer candidate's questions*)
Thank you for your time today.
---
Name:
Signature:
Date:

NOTE:
If the patient asks questions about the procedure itself, refer them to the appropriate service:

| | |
|---|---|
| General Surgery | 910.450.4760/910.450.4761 |
| Orthopedics | 910.450.4820/910.450.4821 |
| Gynecology | 910.450.4561 |

**13.2 Compensation for Participation:**

None.

**13.3 Please describe the pre-screening process. If no pre-screening, enter Not Applicable in the text editor**

Each calendar week, the PI will examine the scheduled surgery list for upcoming procedures for which the PI is the anesthesiologist performing general endotracheal anesthesia. The PI will review the procedure scheduled to determine if the patient is a potential candidate.

A HIPAA waiver has been submitted.

**13.4 Consent Process: Revised Common Rule, Section 219.116: General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section. Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.**

Are you requesting a waiver or alteration of informed consent?

○ Yes ◉ No

Please explain the consent process:

The consent procedure will be performed by the study PI.

The PI will review his upcoming schedule weekly to identify patients who are undergoing procedures with expected duration of less than 3 hours, not of the head, neck or throat, and require general endotracheal anesthesia. A HIPAA waiver will be filed for the PI to review the charts of these potential candidates to confirm basic eligibility (such as age, ASA status and pregnancy status) and to collect the most recent phone number with which to contact patients.

Once the PI has identified eligible candidates, he will contact the candidate via telephone. The PI will explain the study methodology and its objectives. If the study candidate is amenable to participation, the PI will discuss the information contained in the informed consent document and explain the consent and study processes. The study candidate will be given an opportunity to discuss and ask any questions.

If the potential candidate expresses interest in participating in the study, they will be provided with an electronic copy of the informed consent document (ICD) via email or the file transfer system of their choice. This will allow the candidate time to consider their choice to participate in the study and allow them time to review the document before signing. Furthermore, contact information for the investigators will be provided in the event the study candidate requests further elaboration in the time interval between recruitment and day-of-surgery.

On the day-of-surgery, prior to the procedure or administration of any sedating medications, the PI will briefly restate the study goals and procedures, using the informed consent document as a guide. He will ensure that all questions and concerns of the potential candidate are addressed. If the candidate volunteers to participate, the informed consent document will be signed by the participant and PI.

The participant will be enrolled in the study and the PI will assign the participant a Study ID number.

**13.5 DoDI 3216.02 requires an ombudsman to be present during recruitment briefings when research involves greater than minimal risk and recruitment of Service members occurs in a group setting. If applicable, you may nominate an individual to serve as the ombudsman.**

◉ N/A
○ Propose ombudsman

**13.6 Withdrawal from Study Participation:**

Explain the process for withdrawal and specify whether or not the subjects will be given the opportunity to withdraw their data their data/specimens in the event they wish to withdraw from the study

Participants will be able to withdrawal from the study up until they undergo general anesthesia. If the participant withdrawals before the administration of anesthesia, their data will not be collected.

Participants with whom anesthesiologists encounter difficult mask ventilation or difficult intubation will be excluded from analysis. No further study data will be collected. Extubation will be performed with a deflated cuff technique.

## 14.0 Risks and Benefits

### 14.1 Risks of Harm:

Identify all research-related risks of harm to which the subject will be exposed for each research procedure or intervention as a result of participation in this study. Consider the risks of breach of confidentiality, psychological, legal, social, and economic risks as well as physical risks. Do not describe risks from standard care procedures; only describe risks from procedures done for research purposes

## Potential Harms Associated with the Research Study

Breach of confidentiality is always a risk of conducting research.

## Potential Harms Associated with the Intervention

The literature does not currently support the unsubstantiated concern that ICE causes significantly more laryngeal injury than DCE.

The current standard anesthetic practice for extubation is to deflate the endotracheal tube cuff using a syringe prior to extubation [1]. While commonplace and nearly universally accepted, this practice is not based on evidence from randomized controlled trials [2] but is instead due to concern for laryngeal or vocal cord injury and arytenoid cartilage dislocation [3]. However, no publications exist in the medical literature that attribute laryngeal trauma directly to inflated cuff endotracheal tube extubation, as opposed to the process of extubation in general [4]. To the contrary, case reports that describe peri-operative extubation with unintentionally inflated cuffs all note the absence of negative outcome [5, 6].

Within the intensive care setting, unplanned extubation (including accidental extubation and self-extubation) occurs at a rate of 3% to 16% of intubated patients or 0.1 to 3.6 per 100 days of mechanical ventilation [113, 14, 15, 16]. Estimates of national hospitalizations requiring mechanical ventilation approach 800,000, thereby placing the estimated number of unplanned extubations between 24,000 and 128,000 [17]. Presumably, the majority of these unplanned extubations are with inflated cuffs, and yet still no epidemic of laryngeal trauma from inflated cuff extubation exists. Furthermore, there have been no significant differences in laryngeal complications reported between planned and unplanned extubation in the intensive care population, suggesting that it is the endotracheal tube itself (and the process of placing it) that confers the risk of laryngeal complications, rather than the circumstances of its removal [18, 19].

Thus, we have no substantiated reason to believe that there are additional risks of harm in the ICE arm as compared to the DCE arm.

## Potential Harms Associated with the Outcome Assessments

Airway contamination in non-obstetric adults, as defined as: 1] the detection of non-respiratory secretions in the trachea, bronchi or bronchioles, 2] development of new pulmonary symptoms, or 3] new abnormalities in chest radiographs within 24 hours following surgery, is an extremely rare complication of anesthesia.

To assess airway contamination, we are conducting an anterior-posterior chest x-ray to detect contrast material. This procedure is not standard of care, as it is typically only performed when aspiration is suspected. For the purposes of research, we will be performing x-rays on all patients regardless of suspected aspiration. Thus, there are potential risks associated with the administration of the contrast material and the chest x-ray.

### Contrast Material (Iohexol)

By examining all patients regardless of symptoms, we are potentially subjecting patients to contrast aspiration to which they would not be otherwise exposed. While we have no reason to believe contrast would be aspirated at a different rate than oropharyngeal contents, to minimize these risks, we will use iohexol as the contrast material, which has fewer complications as compared to barium and is the preferred contrast material when aspiration is a risk [24-30]. One accidental bronchography was obtained during the conduct of an iohexol-based swallow study in which 10 ml of iohexol was aspirated [35]. That patient experienced no respiratory distress and required no supplemental oxygen administration. Iohexol has an excellent safety profile even when deliberately introduced into the airway, as it is for tracheobronchography. Case series describing iohexol for tracheobronchography encompass neonatal, pediatric, and adult patients under general anesthesia or sedation [31-34]. These case series all emphasize that no deteriorations in respiratory status were observed.

Furthermore, it is possible that the patient may have an acute adverse reaction to the contrast agent. Iohexol is known for its lower likelihood of severe allergic reactions or other adverse events. The known potential complications using iohexol include nausea, vomiting, coughing, or headache. Hives and fever are rare, and life-threatening adverse events are rarely reported with iohexol. [46-49]

### Chest X-Ray

The risks associated with x-rays are minimal. Radiographs do expose patients to radiation. No direct epidemiological data exists to support an increased cancer risk from exposure to the amount of radiation from a single chest x-ray, which is approximately 0.1mSv [50].

It is also possible that the chest x-ray may identify an incidental or unexpected finding unrelated to the study goals. These incidental findings may lead to further tests or evaluation.

**14.2 Measures to Minimize Risks of Harm (Precautions, safeguards):**

For each research procedure or intervention, describe all measures to minimize and/or eliminate risk of harms to subjects and study personnel

Two anesthesiologists will be present at the time of extubation for airway intervention if necessary. The contrast material will only be instilled into the oropharynx after confirmation of endotracheal tube cuff inflation to a seal-generating pressure. Residual contrast material in the oropharynx will be cleared by suctioning prior to extubation. While no contrast material is entirely benign to the lungs, iohexol (Omnipaque) has been selected as the contrast agent likely to pose the lowest overall risk. It is a water-soluble non-ionic agent with animal and human data supporting its safety for bronchograms and swallowing studies assessing for aspiration.

A Speech Pathologist will be the primary data collector for the post-operative day one data, allowing for prompt specialist evaluation in the event of significant laryngeal symptoms.

To reduce the risks of breach of confidentiality, data management precautions, as outlined in section 10.14 will be taken.

**14.3 Confidentiality Protections (for research records, data and/or specimens):**

Describe in detail the plan to maintain confidentiality of the research data, specimens, and records throughout the study and at its conclusion (e.g., destruction, long term storage, or banking). Explain the plan for securing the data (e.g., use of passwords, encryption, secure servers, firewalls, and other appropriate methods). If data will be shared electronically with other team members/collaborators outside the institution, describe the method of transmission and safeguards to maintain confidentiality. Explain whether this study may collect information that State or Federal law requires to be reported to other officials or ethically requires action, e. g., child or spouse abuse

To reduce the risk of breach of confidentiality, data management precautions, as outlined in section 10.14, will be taken.

**14.4 Potential Benefits:**

Describe any real and potential benefits of the research to the subject and any potential benefits to a specific community or society

If the individuals in the research are considered experimental subjects (per 10 USC 980), and they cannot provide their own consent, the protocol must describe the intent to directly benefit all subjects

Based on an animal model, inflated cuff extubation may reduce airway contamination by oropharyngeal fluid. Tracheal aspiration, even micro-aspiration by orophearyngeal secretions, may increase the risk of pneumonia and other pulmonary complications. Leaving the endotracheal tube cuff inflated may effectively generate a vital capacity breath during extubation, maximizing oxygen reserves and facilitating an secretion-clearing cough. These theorized advantages may prolong the time to which supplemental oxygen is required as well as decrease airway/respiratory complications in the immediate post-extubation period.

**14.5 Privacy for Subjects:**

Describe the measures to protect subject's privacy during recruitment, the consent process, and all research activities, etc.

Patients undergoing scheduled surgeries will be recruited over the phone and the consent will be signed prior to surgery. NMCCL has established protocols for protecting patient privacy during phone calls and in the hospital, both of which will be followed during the applicable research activities. All staff involved in the research study have up to date HIPAA training.

Furthermore, to reduce the risk of breach of confidentiality, data management precautions, as outlined in section 10.14, will be taken.

**14.6 Incidental or Unexpected Findings:**

Describe the plan to address incidental findings and unexpected findings about individuals from screening to the end of the subject's participation in the research. In cases where the subject could possibly benefit medically or otherwise from the information, state whether or not the results of screening, research participation, research tests, etc., will be shared with subjects or their primary care provider. State whether the researcher is obligated or mandated to report results to appropriate military or civilian authorities and explain the potential impact on the subject

Should there be an incidental finding or adverse event, the Anesthesia staff, Data Monitor and PI will be immediately notified. The patient will then be fully evaluated and treated with appropriate consultations at NMCCL. As all participants are Tricare eligible by design, any and all necessary care will be covered by Tricare.

Adverse events will be reported to the IRB as per the CID SOPs.

The PI will be the ordering physician for all chest x-rays. The results will then be reported to the PI. The PI will then call the patient with any abnormal findings of concern and document a t-con in MHS Genesis for review by their PCM.

## 15.0 Study Monitoring

**15.1 Your study requires either Data and Safety Monitoring Plan (DSMP) or a Data and Safety Monitoring Board (DSMB).**

- (•) DSMP
- ( ) DSMB
- ( ) Both
- ( ) Not Applicable

A DSMP should describe the plan to monitor the data to verify that the data are collected and analyzed as specified in the protocol. Include who will conduct the monitoring, what will be monitored, and the frequency of monitoring. It should also include the plan to ensure the safety of subjects

Though there have been no randomized controlled trials to assess the differences between ICE and DCE, literature does not currently support the unsubstantiated concern that ICE causes significantly more injury than DCE. Therefore, given the low risk of the intervention as compared to the control arm, there will be no data monitoring committee.

However, to ensure patient safety and data integrity, we will have a Data Monitor. The Data Monitor will be responsible for reviewing severe adverse events that require specialty consults, spot checking data entry for accuracy, and confirming that study protocols are being followed.

## 16.0 Reportable Events

**16.1 Reportable Events: Consult with the research office at your institution to ensure requirements are met. Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event.**

Consult with the research office at your institution to ensure requirements are met

• Describe plans for reporting expected adverse events. Identify what the expected adverse events will be for this study, describe the likelihood (frequency, severity, reversibility, short-term management and any long-term implications of each expected event)

• Describe plans for reporting unexpected adverse events and unanticipated problems. Address how unexpected adverse events will be identified, who will report, how often adverse events and unanticipated problems will be reviewed to determine if any changes to the research protocol or consent form are needed and the scale that will be used to grade the severity of the adverse event

Expected complications of extubation include respiratory complications (coughing, hypoxemia, airway obstruction, bronchospasm, stridor, and laryngospasm), laryngeal complications (hoarseness, dysphonia, sore throat, cough, and dysphagia), asymptomatic airway contamination, or supplemental oxygen. These complications will not be reported as they are expected and related to the process of extubation, which all participants will be undergoing.

The following research related complications will be reported:

- Symptomatic airway contamination (Incidence of 0.006%)
- Severe reaction to iohexol (Incidence 0.04%)

The following potential severe complications of extubation will be reported:

- Severe complications of general anesthesia, such as stroke (Incidence of 0.52% to 0.77%)
- Reintubation (Incidence of 0.1%)
- Unplanned ICU Admission (Incidence of 0.17%)
- Death (Incidence of 0.001%)

The aforementioned adverse events and any unanticipated problems will be reported within 3 business days to the IRB of record as required by NMCCL's CID SOPs.

## 17.0 Equipment/non-FDA Regulated Devices

**17.1 Does the study involve the use of any unique non-medical devices/equipment?**

○ Yes ◉ No

## 18.0 FDA-Regulated Products

**18.1 Will any drugs, dietary supplements, biologics, or devices be utilized in this study?**

- ☐ Drugs
- ☐ Dietary Supplements
- ☐ Biologics
- ☑ Devices
- ☐ N/A

**18.3 Device Details:**

- ☐ Are device(s) in this research being used in accordance to the approved labeling?
- ☑ Are device(s) in this research being used in a manner other than its approved labeling?

When adding a device indicate in the details section of the device if the use is either used in accordance to the approved labeling or in a manner other than it's approved labeling

| View Details | Device Name |
|---|---|
| ⊟ | Teleflex Sheridan/HVT Murphy Eye Endotracheal Tube (Sizes 7.5/7.0) |

| | |
|---|---|
| Manufacturer/Supplier of Device | Teleflex Sheridan |
| Where will the Devices Be Stored | |
| Will Devices be supplied at no Cost | Yes |
| Is this a HUD (HDE) | No |
| HDE Number | |
| Who holds the IDE | N/A |
| IDE details | |

**18.4 Reporting Requirements for FDA-regulated research under IND and IDE:**

Describe the process for complying with FDA regulatory requirements for adverse event reporting and adverse device effects reporting to the sponsor

N/A

**18.5 Sponsor (organization/institution/company):**

- ☑ N/A

If applicable, provide sponsor contact information:

## 19.0 Research Registration Requirements

### 19.1 ClinicalTrials.gov Registration:

- ○ Registration is not required
- ◉ Registration pending
- ○ Registration complete

### 19.2 Defense Technical Information Center Registration (Optional):

- ◉ Registration is not required
- ○ Registration pending
- ○ Registration complete

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**20.2 Abbreviations and Acronyms:**

**NAVAL MEDICAL CENTER CAMP LEJEUNE**

# CONSENT TO PARTICIPATE IN RESEARCH

**Research Title:** *A single-center, patient- and assessor-blinded, randomized controlled trial to compare patient outcomes between Deflated and Inflated Cuff Endotracheal Extubations proceeding scheduled, non-airway surgery in healthy adults (DICEE)*

**Principal Investigator:** CDR Michael Lee MD

You may be able to take part in this research study. This form gives you important information about the study.

Please take time to carefully look over this information. You should talk to the research team about the study and ask them any questions that you have. You can also talk to other people like your friends, family, or your personal doctor about whether or not to take part in this study.

**Participation is voluntary. You do not have to take part in this research**. It is your decision. You can also choose to stop participating at any time during the study.

## 1. KEY INFORMATION

*General anesthesia* is a treatment with medicine to make you unconscious for your surgery, so that your body will be completely still. This is sometimes called "being put to sleep" or "being put under."

Most of the time, we use a breathing tube to help a machine breathe for you. The breathing tube has a *cuff*, which is like a small balloon. After the breathing tube is put in your airway, the cuff is inflated. This keeps the breathing tube in place and keeps fluids like saliva and stomach juices from getting into your airway. When we remove the breathing tube, that is called *extubation*.

Normally, doctors deflate the cuff before removing the breathing tube. This is called **deflated cuff extubation**. Some doctors worry that keeping the cuff inflated while it is removed can hurt your throat or vocal cords.

However, some doctors keep the cuff inflated when removing the breathing tube. This is called **inflated cuff extubation**. These doctors think that keeping the cuff inflated can help keep fluids from entering your airway.

Doctors have not studied if deflated cuff extubation is better or worse than inflated cuff extubation. The goal of this study is to see which type of extubation is better at keeping fluids from getting in your airway.

If you choose to take place in this study, you will get general anesthesia and have your surgery as planned. Near the end of your surgery, we would place a small amount of liquid at the back of your mouth. This liquid is called contrast material, and it is like a dye. The contrast material will help us find out if any liquid enters your windpipe or lungs. Then we will remove as much of the contrast material as we can, along with any other fluids, using our normal methods.

When it is safe to take the breathing tube out, we will either do a deflated cuff extubation or an inflated cuff extubation. This decision will be made at random, like by the flip of a coin.

Information will be collected about you, your surgery, and how well you are breathing. After surgery, we will take a chest x-ray to see if any of the contrast material is in your windpipe or your lungs. Otherwise, everything else after your surgery would be normal. 24 to 48 hours after your surgery, a member of the research team will ask you about any symptoms you might have, like sore throat or a hoarse voice. That would be the end of the research study for you. You would follow up with your surgeon as planned.

**Taking part in this study is optional.** If you choose to take part, you will be in the study from the time you come into the hospital for surgery until about 24 to 48 hours after surgery.

There are risks any time you have a breathing tube removed after general anesthesia. However, there is no proof that the risks are different between deflated cuff extubation and inflated cuff extubation. It is possible, but unlikely, that you might have a reaction to the contrast material, such as an allergic reaction or a sore throat.

Also, the chest x-ray you would receive for this study uses a small amount of radiation. We are all exposed to radiation from natural sources every day, but any exposure to radiation can increase the risk of cancer over your lifetime. The amount of radiation from one chest x-ray is about the same you get from 10 days of daily life.

There are no guaranteed benefits to being in this study. However, you might be less likely to get fluids in your windpipe or lungs.

If you choose not to take part in this study, you will get general anesthesia and have your surgery as planned. Your doctor will determine whether to do deflated or inflated cuff extubation based on their experience and judgment.

**Your decision will not affect your future care at Naval Medical Center Camp Lejeune (NMCCL).** If you decide to take part in this research study, you will be asked to sign this document. Before you sign, be sure you understand what the research study is about. Please read all sections of the consent form, including the risks and possible benefits to you.

Please tell the researchers if you are taking part in another research study.

## 2. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY AND WHO IS BEING ASKED TO TAKE PART?

You are being asked to take part in this research study because you are having surgery under general anesthesia.

*General anesthesia* is a treatment with medicine to make you unconscious for your surgery, so that your body will be completely still. General anesthesia also keeps you comfortable and controls your pain during the surgery. This is sometimes called “being put to sleep” or “being put under.”

Most of the time, doctors will use a breathing tube to help a machine breathe for you. The breathing tube has a *cuff*, which is like a small balloon. After the breathing tube is put in your windpipe, the cuff is inflated. This keeps the breathing tube in place and keeps fluids like saliva and stomach juices from getting into your airway.

Your airway includes your windpipe and lungs. There are some cases when fluids can get into your airway, and you will still be fine. In other cases, when fluids get into your airway, the germs and bacteria can make you sick or hurt your lungs. Whether or not the fluid in your airway is harmful, it is called *airway contamination*.

When we remove the breathing tube, that is called *extubation*.

Normally doctors deflate the cuff before removing the breathing tube. This is called **deflated cuff extubation**. Some doctors worry that keeping the cuff inflated while it is removed might hurt your throat or vocal cords. However, there have not been studies to see if this is true.

Some doctors keep the cuff inflated when removing the breathing tube. This is called **inflated cuff extubation**. These doctors think that keeping the cuff inflated can help keep fluids from entering your airway.

Doctors have not studied if deflated cuff extubation is better or worse than inflated cuff extubation. The main goal of this study is to see which type of extubation is better at keeping fluids from getting in your airway. We will also look to see which type of extubation is better or worse at keeping you from having normal side effects of extubation, like a sore throat, coughing, or need for extra oxygen.

## 3. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH AND HOW LONG WILL IT TAKE?

There will be about 88 people taking part in the study at NMCCL over about 12 months. This study will take place for up to a week before the day of surgery (DOS) until 24 to 48 hours postoperative.

This study is looking at inflated cuff extubation. Inflated cuff extubation is when the balloon-like cuff of the breathing tube used during general anesthesia is removed while it is still inflated. Inflated cuff extubation has not been well-studied, because some doctors are worried that the inflated cuff could hurt someone’s throat or voice box. There haven’t been studies that show whether or not this is true.

If you choose to take part in this study, you will be in the study from the time you sign this document until about 24 to 48 hours after surgery. You will not have to make any extra hospital or doctor visits.

As part of the study, you will:

- Have some information about you, like your age, biological sex, weight, height and medical history used for research.
- Have liquid contrast material placed into your mouth while you are under general anesthesia.
- Be assigned at random to one of the two extubation groups. Randomization is a process like flipping a coin and means you will have a chance of being assigned to either of the groups.

  - If you are in the **deflated cuff extubation** group, all air will be removed from the breathing tube cuff before the breathing tube is taken out.
  - If you are in the **inflated cuff extubation** group, air will be left in the breathing tube cuff when the breathing tube is taken out.
- Have information about your general anesthetic, your surgery, and your recovery used for research. This will include things like if you have a sore throat, trouble swallowing, or need extra oxygen.
- Receive a chest x-ray after the surgery.
- Have a research team member ask you about your voice and throat 24 to 48 hours after your surgery. They will call you on the phone if you are home or visit your room if you are still in the hospital.

This study is *blinded*. For this study, it means that you will not know what group you are in. The people who will collecting information about after the procedure will also not know what group you are in. The only person who will know what group you are is Dr. Lee, because he will be doing the extubation. If there is an emergency, Dr. Lee will let people know what group you were in.

When the study is complete, the results of the study will not be automatically shared with you. But if you want to know the results, you can ask Dr. Lee about the study.

## 4. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

Whether or not you take part in this study, there are risks from having using a breathing tube. But doctors do not know for sure if the risk of side effects from inflated cuff extubation is better, worse, or the same as deflated cuff extubation.

Common, but not serious risks from using a breathing tube can include:

- Trouble swallowing,
- Coughing,
- Painful or sore throat,
- Hoarse or weak voice,
- Swelling in your voice box,
- Bruising on or around your voice box,
- Being unable to move or use your voice box, or
- Parts of your voice box moving out of place.

These side effects happen in about 1 of every 3 patients who need a breathing tube for surgery. Some side effects can be mild and go away quickly. Other side effects can be more serious and permanent. Serious side effects are rare and happen in about 1 out of every 1,000 patients.

We do not know if these risks will be more or less common if you take part in this study.

To find out if fluids get in your airway, we are using contrast material and a chest x-ray. These both come with risks. You could be allergic to the contrast material, which could cause you to have mild problems, like feeling itchy, or severe problems, like not being able to breath. The contrast material may cause flatulence, diarrhea, nausea, vomiting, headache, or abdominal pressure from entering your

stomach. The contrast material might also bother your airway, causing cough, wheezing, shortness of breath, fever, or uncomfortable breathing. About 1 to 3 patients in 100 may have minor side effects like these from the contrast material. More serious side effects can happen in about 1 in 2,500 patients. Depending on the symptoms and severity, treatment may be required for any contrast material side effects.

The chest x-ray you would receive for this study uses a small amount of radiation. We are all exposed to radiation every day. However, any exposure to radiation can increase your lifetime risk of cancer. The amount of radiation from one chest x-ray is about the same you get from 10 days of daily life.

The chest x-ray could also find problem that you didn't know about. This might mean you have to have more tests or doctors' visits related to this new problem.

We make special efforts to protect your information. There is always a risk that someone who shouldn't could get ahold of information in your medical records or other information that is collected for research.

There may also be other risks of taking part in this study that we do not yet know about.

## 5. ARE THERE BENEFITS TO TAKING PART IN THIS RESEARCH STUDY?

There may or may not be a direct benefit to you by taking part in this research study. Studies done in animals show that you might be less likely to get fluid in your airway. You may also be less likely to need extra oxygen after extubation. However, there is no guarantee that you will benefit from being in this research.

## 6. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

Your alternative is to not take part in this study. If you choose not to take part, your anesthesia doctor will choose an extubation method based on their experience and judgment.

## 7. WILL YOU GET PAID FOR TAKING PART IN THIS RESEARCH STUDY?

No, you will not receive any compensation for participating in this study.

## 8. ARE THERE COSTS FOR TAKING PART IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

## 9. IS THERE A SOURCE OF FUNDING?

No funding is being provided for this research study.

## 10. WHAT IS THE LOCATION OF THE RESEARCH?

Everything related to this study is going to take place at Naval Medical Center Camp Lejeune.

## 11. ARE THERE ANY DISCLOSURES OF FINANCIAL INTERESTS OR OTHER COMMERCIAL RELATIONSHIPS?

The research study team doesn't get any money for doing this research from companies or other funding groups.

## 12. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Your records related to this research study may only be shared in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. You can locate and read the form online or a copy of the form can be given to you upon request. (Online at: https://www.esd.whs.mil/Portals/54/Documents/DD/forms/dd/dd2005.pdf),

The research team will keep your research records. These records may be looked at by staff from the NMCCL's Anesthesiology Department, NMCCL's Clinical Investigations, the Defense Health Agency, and the DoD. The committee responsible for protecting research participants, called the Institutional Review Board (IRB), may also look at your records as part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to:

- Locking paper copies of research data behind two locks. For example, paper will be in a locked office in a locked building, or in a locked cabinet/drawer in a locked office,
- Using a coded number, or study ID number, instead of your name or medical record number on both any research data,
- Saving computer files on the hospital's private network, which:
    - Has a *firewall*, or a protection or barrier in the computer to protect information from being seen by people who shouldn't see it, and
    - Needs *two-factor authorization*, which means that people who are allowed to see the data need both a special access card and a password,
- The computer file that matches your name to your study ID number will have an extra password so that only Dr. Lee will be able to see it.

Researchers will make every effort to protect your privacy and confidentiality. However, there are risks of breach of information security and information loss. The researchers agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

Information gained from your participation in this research study may be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified when your information is shared in these ways; all information will de-identified.

If applicable, a description of this clinical trial will be available online at http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of results. You can search this website at any time.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

## 13. WHAT HAPPENS IF THE RESEARCHERS SEE AN INCIDENTAL FINDING?

It is possible that while looking at your x-ray, the research team might see something strange that they did not expect to see. This is what is called an *incidental finding*.

The research team will let you know if they see an incidental finding. Depending on the type of incidental finding, they may contact you by phone or in person. If it might be serious, the research team will tell you right away.

The research team will also tell your primary doctor about the incidental finding. If you do not have a primary doctor, they will refer you to the right type or doctor for most tests.

- An incidental finding may cause you to feel anxious
- Since an incidental finding will be part of your medical record, it could be harder to get health or life insurance in the future.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study.

Any tests or care you might need because of the incidental finding would not be paid for by this study. You would be responsible for those costs. However, if you are a DoD beneficiary, you will have access to care through the Military Health System and TRICARE.

## 14. WHAT HAPPENS IF YOU WITHDRAW FROM THIS RESEARCH?

The decision to take part in this research study is optional. This means you do not have to take part if you do not want to. You can also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty or loss of benefits to which you are otherwise entitled.

If you do not want to keep taking part in the research study, you must tell Dr. Lee or another member of the research team.

- If you tell the research team you do not want to take part before you have general anesthesia, then you will not be included in the research study at all.
- If you tell the research team you do not want to take part after your surgery, any data that has already been collected will be used for the research study, but we will not collect any more data about you or your health.

Please note that taking back your consent to take part in this research does not take back the HIPAA Authorization that you will sign below. The HIPAA Authorization is how you give us permission to use or reveal your protected health information. To take back your authorization, please send a letter to Dr. Lee.

Dr. Lee may stop you from taking part in this research study at any time if he thinks it is in your best interest. For example, if there are any problems giving your general anesthesia, or if there are any problems with your surgery, Dr. Lee may decide to take you out of the study.

## 15. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have gotten hurt because you were in this research study, you need to tell Dr. Lee. His contact information is below.

A Department of Defense (DoD) *healthcare beneficiary* is someone who is able to get treatment from the Military Health System (MHS). This might be because they are or were in the military, or because their spouse or parent was in the military.

If you are injured because you took part in this research study and you are a DoD healthcare beneficiary, you will be able to get treatment from the MHS for as long as you are DoD healthcare beneficiary. This can include free medical care at a DoD hospital or clinic. If there is not room for you at the closest hospital or clinic, you may have to travel to a hospital or clinic farther away.

Travelling to and from hospitals or clinics will not be provided or paid for by DoD. If you do not have TRICARE insurance, the DoD cannot pay you back for any medicals bills that you might get. You will not get money if you are hurt in this research study.

You are not waiving any legal rights if you sign this form.

# HIPAA AUTHORIZATION

**A HIPAA Authorization is how you give us permission to use or reveal your health information.**

*The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, as implemented by the DoD, permits the MHS to use or reveal your health information with a valid Authorization. The MHS is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force. A valid Authorization must include the core elements and required statements as contained below.*

The information above gives you the information you need to consent, or agree, to take part in the research study. This consent document also describes why we need to use or share your health information.

Below is the information you need to decide if you want to give us permission to use or reveal your health information. Please read it and ask questions about anything you don't understand before deciding to give us permission. If you do not want to give us permission to use and share your health information, you do not have to. However, you will not be able to participate in this research study.

**a. What health information will be used or disclosed?**

- Your name and medical record; which will allow us to order the chest x-ray after your surgery and to look up your results afterwards,
- Your phone number (if you have left the hospital) or room number (if you have not left the hospital); which will allow us to follow up with you 24 to 48 hours after your surgery
- Information about your surgery and the general anesthesia used; which will help us understand who might benefit from this research, and
- How well you feel and any side effects you have after surgery; this will help us compare the two types of extubation.

**b. Who will be authorized to use or disclose (release) your health information?**

Your health information may be use or shared by Naval Medical Center Camp Lejeune (NMCCL), which is sometimes also known as the Navy Medicine Readiness & Training Center at Camp Lejeune.

**c. Who may receive your health information?**

- Study staff who are helping with this research study
- NMCCL's Clinical Investigations Department, which is the department that helps doctors and nurses do research, and
- The Institutional Review Board, which is the group that makes sure research on humans is safe and ethical.

**d. What if you decide not to sign this Authorization?**

You do not have to sign this Authorization, but if you do not, you will not receive research-related treatment. The MHS **will not** refuse treatment that is not part of this study, payment, enrollment, or eligibility for benefits based on whether you sign this Authorization.

**e. Is your health information requested for future research studies?**

No, your health information *is not* requested for future research studies.

**f. Can you access your health information during the study?**

You may have access to your health information at any time, unless your identifiers are permanently removed from the data.

**g. Can you take back this authorization?**

- You may change your mind and take back your Authorization at any time. However, if you take back this Authorization, any person listed above may still use or share any already obtained health information as necessary to maintain the integrity or reliability of this research.

- If you take back this Authorization, you may no longer be allowed to take part in this research study.

- If you want to take back your Authorization, you must write to:

  CDR Michael Lee MD
  Naval Medical Center Camp Lejeune
  Department of Anesthesia and Pain Medicine
  100 Brewster Blvd
  Camp Lejeune, NC 28745

**h. Does this Authorization expire?**

Yes, it expires at the end of the research study.

**i. What else may you want to consider?**

- No publication or public presentation about the research described above will reveal your identity without another signed Authorization from you.
- If all the information that does or can identify you is removed from your health information, the remaining de-identified information will no longer be subject to this Authorization and may be used or shared for other purposes.
- In the event your health information is disclosed to an organization that is not covered by HIPAA, the privacy of your health information cannot be guaranteed.

# CONTACT INFORMATION

**Principal Investigator (PI)**

The Principal Investigator or a member of the research study team will be available to answer any questions throughout this study.

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| **Principal Investigator**: | CDR Michael Lee MD |
| Phone: | (910) 450-4786 |
| Mailing Address: | Naval Medical Center Camp Lejeune<br>Department of Anesthesia and Pain Medicine<br>100 Brewster Blvd<br>Camp Lejeune, NC 28745 |
| **Clinical Research Coordinator**: | Kathiusca Chalas-Reid BS |
| Phone: | (910) 450-5082 |
| Mailing Address: | Naval Medical Center Camp Lejeune<br>Clinical Investigations Department<br>100 Brewster Blvd<br>Camp Lejeune, NC 28745 |

**Naval Medical Center Portsmouth (NMCP) Human Research Protection Program (HRPP) Office**

The Human Protections Administrator (HPA) will be available to answer questions or discuss concerns you may have about this research study.

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| Human Protections Administer: | Chemely Walker MS |
| Phone: | (910) 450-3460 |

**Institutional Review Board (IRB) Office**

If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, you can contact the office responsible for ensuring research participant protection, the Institutional Review Board (IRB).

Naval Medical Center Portsmouth
620 John Paul Jones Circle
ATTN: CID
Portsmouth, VA 23708
(757) 953-5939
usn.hampton-roads.navhospporsva.list.nmcp-irboffice@health.mil

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE RESEARCHER BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL DOCTOR OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated photocopy of this document will be given to you.

# SIGNATURES

## SIGNATURE OF PARTICIPANT

Your signature below indicates that:

- You authorize the Military Health System to use and reveal your health information for the research purposes stated above as described in the HIPAA Authorization;
- You have read (or someone has read to you) the information in this consent including the HIPAA Authorization;
- You agree that you have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to you. You have been provided with the opportunity to ask questions
- You voluntarily consent to take part in this research study.

By signing this form, I have not given up any of my legal rights as a research participant.

_____
Printed Name of Participant

_____ ____/____/____
Signature of Participant Date (DDMMMYYYY)

## SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT

(Can only be signed by an investigator approved to administer consent)

_____
Printed Name of Administering Individual

_____ ____/____/____
Signature of Administering Individual Date (DDMMMYYYY)