Study Title: Flexible Intubation Scope vs. Flexible Intubation Scope and Video Laryngoscopy Combination: A Prospective Randomized Clinical Trial

Principal Investigator: Carin A. Hagberg M.D.

Co-Investigator(s): Uduak U. Williams M.D., Carol Lewis M.D.

Collaborator(s): Pascal Owusu-Agyemang, M.D., Acsa Zavala, M.D., Neil Bailard, M.D., Antoinette Van Meter, M.D., Peter Hsu M.D., Vivian Porche, M.D., Catherine Vu M.D., (Cancer Airway Group)

Statistician: Mike Hernandez

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SUMMARY TABLE

Title	**Flexible Intubation Scope vs. Flexible Intubation Scope and Video Laryngoscopy Combination: A Prospective Randomized Clinical Trial**
Project Office	Department of Anesthesiology, Critical Care and Pain Medicine, MD Anderson Cancer Center.
Study Size (# of patients)	120
Study Design	This study will be a prospective randomized clinical trial.
Primary Objective	• To compare the rates of difficult Endotracheal Tube (ETT) placement using a Flexible Intubation Scope (FIS) versus a combination of flexible intubation and video laryngoscopy (VL/FIS) in difficult airway management.
Primary Outcome	• Difficult ETT placement is defined as: (i.) either first intubation time >60 seconds or (ii.) first attempt failure at intubation or (iii.) ease of intubation reported as difficult by provider.
Secondary Objectives	• To compare the ease of using a flexible intubation scope (FIS) with and without the use of the video laryngoscope (VL) • Total time to secure the airway • Number of attempts required for intubation • Rate of failure at intubation • Incidence of desaturation • Assessment for hoarseness, sore mouth, neck, or jaw, dysphonia, dysphagia, lip injury, tongue injury, or tooth damage.
Inclusion Criteria	• Ages $\geq$ 18 years of age • All surgical patients with known or suspected difficult airways that meet at least three (3) of the Difficult Airway criteria [Mallampati III-IV, Neck circumference > or = 40 cm, Sternomental distance < 12 cm, Thyromental distance < 6 cm, Mouth opening < 4 cm, BMI $\geq$ 35 kg/m^2, Upper Lip Bite Test - ULBT (class III)] or history of radiation to the head or neck area • American Society of Anesthesiology (ASA) I-IV • Has provided written informed consent
Study Procedures	• Initial study assessments will be performed in the preoperative holding area. All study interventions will be performed in the operating room prior to the first surgical skin incision. Postoperative assessments will be conducted in PACU. • Patients will be randomized to either study group using OnCore. **Group A: FIS (control), Group B: VL/FIS (intervention)**. After the patient provides consent and is enrolled into the study, they will be randomized to a study group. The study team will inform the attending anesthesia

	provider about the group the patient was assigned and the instruments to be utilized during intubation. • Following induction of general anesthesia and adequate manual ventilation, the anesthesia provider will attempt to successfully intubate the patient utilizing, a FIS or a combination of FIS and VL. No more than 2 intubation attempts shall be made. If necessary, in between intubation attempts, adequate patient ventilation will be performed prior to the next intubation attempt. • For both the control and intervention groups, the anesthesia provider will be given the option to secure the airway via oral pathway (passage) according to clinical judgment. If a patient's airway has not been secured within 2 attempts of the respective, allocation treatment, a third attempt will be made utilizing another technique or device (as a rescue attempt) at the discretion of the anesthesia provider. At this point, no further study data will be collected, except of what device was used for the rescue attempt and any potential Adverse Events.
Brief Analysis Plan	**For Primary Objective:** A total of 60 patients will be randomized to each intervention arm (a total of n = 120 patients). • With 60 patients per study arm, a 2-sided chi-square test with alpha = 0.05, and an assumed rate of difficult ETT of 30% on the control arm, then a minimum detectable difficult ETT rate of 10% (an absolute difference of 20 percentage points) would be considered statistically significant (nQuery v7) with power of 80%. • For each study arm consisting of 60 evaluable patients (120 patients total), estimated rates of difficult ETT will be provided using exact 95% CI using the method of Clopper-Pearson. For example, a rate of 25% would provide exact 95% confidence interval limits that do not exceed (0.15 0.38), exact 99% CI limits that do not exceed (0.12, 0.42) using the method of Clopper-Pearson. **For the Secondary Objective:** To evaluate ease of use, each of the 3 dimensions described below will be assessed independently. First, the time of intubation will be assessed for distributional assumptions using histograms, stem and leaf plots, and box plots. Descriptive statistics such as the median and range or the geometric mean ± SD will be used to summarize the data. Second, ordinal data describing the number of attempts will be summarized using the median and range; and third, the

	number of complications will be summarized using the median and range. For number attempts and complications, frequencies and percentages will be used if the maximum number is small (≤ 4 attempts or complications). Comparisons between continuous covariates of interest will be conducted using a t-test, or Wilcoxon rank-sum test if more appropriate. Categorical covariates will be compared using chi-square or Fisher's exact test. **Exploratory Analyses:** Depending on the distributional assessment of outcomes for each of the 3 items: i) time of intubation, ii) number of attempts, and iii) the number of complications, a total score will be derived for each patient. Each outcome will be translated into a binary scale. For example, starting with intubation time, the completion a procedure within 60 seconds will be assigned a '0', and completion taking more than 60 seconds will assign a '1'. For the number of attempts, we will assign a '0' for a single attempt and a '1' for more than a single attempt. And finally for complications, we will assign a '0' for no complication arising and a '1' for any complications arising. The total score will range from 0 to 3 and will be summarized using frequencies and percentages related to each level of the total score and using the mean score and standard deviation, whichever is more appropriate. Other exploratory outcomes include: Ease of ETT insertion (ranked on a 1 to 5 scale as described in Section 5.4) and will be summarized using descriptive statistics. These exploratory study outcomes will be compared between treatment arms using an independent samples t-tests or chi-square tests. Potential cut-points for these exploratory outcomes may be considered to inform if low versus high scores are associated with select patient outcomes of interest. Cumulative incidence plots will be used to visualize time to intubation, if appropriate. Multiple logistic regression analyses will be conducted to assess the association between any dichotomous outcomes of interest and type of intervention after adjusting for select covariates of interest.

1.0 OBJECTIVES

1.1 Primary Objective:

- To compare the rates of difficult Endotracheal Tube (ETT) placement using a flexible intubation scope (FIS) versus a combination of flexible intubation and video laryngoscopy (VL/FIS) in difficult airway management.

1.2 Secondary Objectives:

- To compare the ease of using a flexible intubation scope (FIS) with and without the use of the video laryngoscope (VL)
- Total time for securing the airway
- Number of attempts required for intubation
- Rate of failure at intubation
- Incidence of desaturation
- Assessment for hoarseness, sore mouth, neck, or jaw, dysphonia, dysphagia, lip injury, tongue injury, or tooth damage.

1.3 Exploratory Objective:

- To assess the utility of using a total score for summarizing 3 dimensions that characterize ease of ETT insertion: i) time of intubation, ii) number of attempts, and iii) the number of complications.

2.0 BACKGROUND

2.1 Difficult airway in patients with head and neck tumors

Head and neck cancers include tumors of the oropharyngeal cavity, larynx, paranasal sinuses, thyroid and salivary glands.[1] A failure to recognize and to properly manage the airway in this population may lead to significant morbidity and mortality. Patients with head and neck tumors have a higher risk of difficult airways compared to the general population (15.75% vs. 2.5%).[7] In the Fourth National Audit Project (NAP4) of the UK; a large population based study of airway complications Woodall et al. discussed the difficult airway in the head and neck population with 39% of major airway complications occurring in patients undergoing head and neck surgery.[3] In several closed claims analysis studies, patients undergoing head and neck surgery consistently rank among the highest group of patients who experienced an adverse airway related event.[4-6] This may be due to the underlying disease or result from the side effects of treatment (i.e. radiation or surgically induced deformities). Oro-pharyngeal tumors may reduce the amount of space in the oropharynx and result in a difficult direct laryngoscopy. The associated obstructive symptoms may lead to difficulty with ventilation, especially after the induction of anesthesia. Tumors outside the airway, such as large thyroid masses, may produce extrinsic compression or distortion of the trachea or larynx. Radiation induced contractures may also lead to reduced mobility of the neck, and of the tissues of the oropharynx. In addition, radiation induced changes of the larynx may reduce visibility and accessibility of the larynx by conventional laryngoscopy. These changes can be associated with reduced ventilation, which could be exacerbated upon induction of anesthesia.

2.2 Flexible Intubation Scope

The gold standard of care for intubating patients with known difficult airways is an awake flexible intubation scope (FIS).[7] Flexible fiberscopes have long been used for tracheal intubation, especially in cases of a difficult airway. Some of the advantages of using a Flexible intubation scope (FIS) are that it provides a means to view the glottis in instances where standard intubation methods fail. These include patients with limited mouth opening, an unstable cervical spine, head and neck tumors, and trauma to the airway.

Asleep FISs are often employed in head and neck cases where the intubation may be challenging, but the ability to mask ventilate the anesthetized patient is possible. This saves time due to not needing to topicalize the patient's mucosa and also avoids the discomfort to the patient of an awake intubation. Nevertheless, it still requires a great deal of skill on the part of the anesthesiologist and can actually take just as long or longer to intubate than when doing an awake FIS, due relaxation or collapse of the soft tissues of the airway into the path of the FIS, making the pathway to the trachea more obscured.[9]

Despite its value to management of the difficult airway, FIS has its pitfalls, once the scope is placed in the trachea, advancement of the tube is still a blind process. Collapse of the airway post induction of anesthesia can obstruct the view with the scope even with the use of jaw thrust. The ETT may get caught on the arytenoids and forceful placement may traumatize the airway.

2.3 KARL STORZ Intubation Fiberscopes

The new flexible 5.5 x 65 intubation video endoscope from KARL STORZ provides a better overview of the working area. Similar to the C-MAC® video laryngoscope, the 5.5 x 65 scope delivers clear, pixel-free images without a moiré pattern. The 5.5 x 65 endoscope can be directly connected to the C-MAC® monitor. This enables a changeover to the video laryngoscope in a short time, if necessary. The flexible 5.5 x 65 intubation video endoscope is a further component within the C-MAC® system.

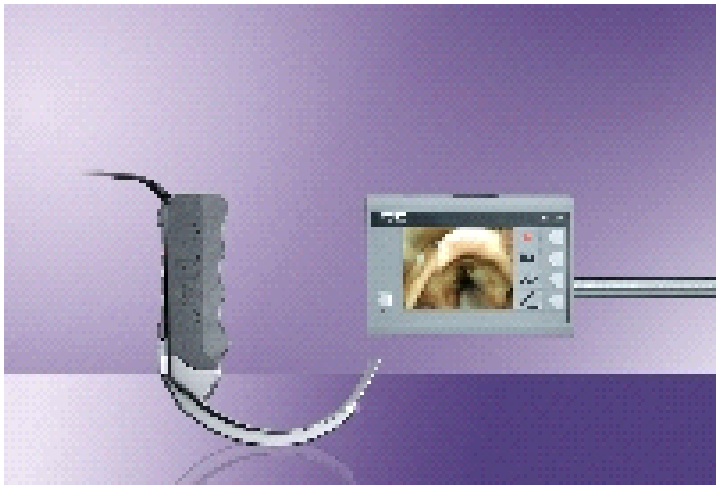
2.4 Video laryngoscopy

Video laryngoscopy (VL) is a method of indirect laryngoscopy using camera technology to visualize airway structures. Incorporating a VL in combination with a FIS enhances the technique of FIS by providing a view above the glottis and thus allowing visualization of the ETT as it is advanced into the airway.[12] Also, the VL will help open the oropharynx and improve the view while providing

complete visualization of the FIS. VL has become the recommended method as the preference in patients with suspected difficult tracheal intubation. Advantages of using VL include the elimination of the need to align the airway axes to provide a line of sight, providing a better view of the glottis especially in cases with limited neck extension or mouth opening, serving as an educational tool allowing other providers to view the airway structures, less hemodynamic response to intubation, and decreased risk of esophageal intubation.[10] Aziz et al. report a 92% success rate with the use of VL as a rescue in patients in whom direct laryngoscopy had failed.[11] In a randomized controlled trial comparing different video laryngoscopes to direct laryngoscopy, Yumul et al. found an improved glottic view using VL compared to standard direct laryngoscopy using a laryngoscope.[13] Lenhardt et al. found a 100% success rate of intubation using the combination of a FIS and a VL on a group of patients with known difficult airways requiring in-line stabilization. [14]

2.5 C-MAC® Video Laryngoscope

The C-MAC® video laryngoscope is available in the original MACINTOSH blade shapes (sizes 2, 3 and 4), the MILLER shape (sizes 0 and 1), and in the blade shape for difficult airways – the D-BLADE™. The MILLER laryngoscopes correspond with the current MILLER form. The design is in line with the European closed form, which ideally satisfies the stringent demands placed on hygiene and ergonomics.



2.6 Rationale

Combined VL and FIS can provide superior conditions for tracheal intubation in patients with head and neck tumors. We hypothesize that the use of the combination technique will improve the time to intubation and also decrease the number of attempts to intubate head and neck patients with known or suspected difficult airways. If our hypothesis is confirmed, a significant large number of patients will benefit (i.e. less trauma, less episodes of hypoxemia and less postoperative sore throat) from the use of this new intubation technique. To test our hypothesis, we plan on conducting a randomized controlled trial using the combination of FIS with VL, comparing it to the use of the FIS alone in patients with known or suspected difficult airways undergoing surgical procedures.

3.0 DISCUSSION OF SUBJECT POPULATION

3.1 Subject Characteristics

Any male and female patients ≥18 years of age, undergoing planned surgery.

3.2 Inclusion and Exclusion Criteria

Inclusion Criteria:

- Ages ≥ 18 years of age
- All surgical patients with known or suspected difficult airways that meet at least three (3) of the Difficult Airway criteria [Mallampati III-IV, Neck circumference > or = 40 cm, Sternomental distance < 12 cm, Thyromental distance < 6 cm, Mouth opening < 4 cm, BMI ≥ 35 kg/m^2, Upper Lip Bite Test - ULBT (class III)] or history of radiation to the head or neck area
- American Society of Anesthesiology (ASA) I-IV
- Has provided written informed consent

Exclusion Criteria:

- Active bleeding from nasopharynx or oropharynx
- Trismus
- Oral pathology obstructing the glottic view
- Planned awake or nasal intubation
- Neuromuscular Blockade (NMB) contraindicated post-induction
- Emergency endotracheal intubation and patients intubated pre and post-surgery
- Surgical procedures such as Tracheostomy, Laryngectomy, Esophagectomy
- Patient refusal or inability to consent for study participation
- American Society of Anesthesiology (ASA) V
- Pregnant females

3.3 Discussion of Subject Population:

Head and neck tumors continue to be very common and a significant number of patients with these tumors present to our practice for surgical care. Wong et al, found a higher incidence of difficult airways in head and neck surgical patients.[8] In the Fourth National Audit Project (NAP4) of the UK, review of cases showed that 39% of all emergent surgical airways were performed in head and neck patients.[3] Therefore, our study is focused on patients who are at increased risk of failed intubation when conventional means are used.

4.0 SUBJECT IDENTIFICATION, RECRUITMENT AND CONSENT:

4.1 Method of Subject Identification and Recruitment

Subjects will be pre-screened in the patient population scheduled for surgery at MD Anderson Cancer Center's Main OR or Mays OR. Advertisements for study subjects are not anticipated. Once a potential subject has been identified, he/she will be approach in the preoperative holding area and asked to sign the study's informed consent document. Then delegated study staff will perform assessments to verify subject's eligibility, which will be confirmed by the PI or Co-I's prior enrollment. Study Staff will follow institutional policy SOP 04: Informed Consent Process.

4.2 Consent Process

Subjects will be explained, in detail, the purpose, their role, and study procedures in relation to what's considered research and standard of care (SOC); as well as the potential risks, benefits and alternatives prior to study enrollment. They will be given a consent form to read and if they so choose, to discuss with friends, family, and other clinicians. They will be invited to ask questions and, after all questions are answered to their satisfaction, invited to sign the consent form. The Principal Investigator or designees (with proper delegation of authority) will participate in the consenting process to ensure the subject has full understanding of the procedure and risks. No study-specific procedure will be performed before the consent form is signed.

Subject participation in this investigation is voluntary. Written informed consent is required from all subjects prior to the subject's participation in the investigation. Also, an obtained permission of the faculty anesthesiologist, in charge of the patient's anesthesia care, must also be granted for subject participation. A signed copy of the consent will be given to the subject. While not anticipated, the PI will report any failure to obtain subject consent to the IRB within 5 days of learning of such an event, as required by regulation.

Prior to participating in this investigation, the site will be required to have an IRB-approved Informed Consent Document. Any modifications to the consent must be approved by the IRB of record.

4.3 Costs to the Subject

None.

4.4 Payment for Participation

None.

4.5 Return of Individual Research Results

Not Applicable.

5.0 METHODS AND STUDY PROCEDURES

5.1 Pre-treatment Evaluation

Screening

Patients will be pre-screened for eligibility prior to their scheduled surgical procedure. Eligibility will be verified in the preoperative holding area.

Randomization

OnCore will be used to randomly assign eligible study participants to either the control group (N = 60) or the study (intervention) group (N = 60). Additionally, the collection of demographic information will take place before anesthetic and surgical care to acquire baseline data information on: age, gender, height, weight, and BMI. Patients will be randomized after consenting and enrolling into the trial, preoperatively, on their scheduled day of surgery.

5.2 Study Procedures

All study interventions will be performed in the operating room prior to the first surgical skin incision. Patients follow up visits will be conducted postoperatively in PACU.

Patients will be randomized in OnCore to one of two groups **- Group A: FIS (control), Group B: VL/FIS (intervention**). After the patient consents and is enrolled into the study, they will be registered in OnCore and then randomized. The study team will inform the attending anesthesia provider about the subject's assigned group prior to surgery.

Pre-Induction: Standard of Care (for both study arms)
In the operating room, standard ASA monitors will be used including a pulse oximeter, an electrocardiogram and a blood pressure cuff. The attending anesthesiologist may elect to place an invasive arterial line for blood pressure measurement. General anesthesia will be induced by intravenous administration of lidocaine (1mg/kg), propofol (1-2 mg/kg), fentanyl (1-3mcg/kg), succinylcholine (1-2mg/kg), or rocuronium (0.5-1 mg/kg). Patients' lungs will be ventilated via facemask 100% oxygen until complete muscle relaxation is achieved.

Post-Induction: Research Procedure (Control group-FIS)
Following induction of general anesthesia and adequate manual ventilation, the anesthesia provider will attempt to successfully intubate the patient utilizing the flexible intubation scope. No more than 2 intubation attempts shall be made. If necessary, between intubation attempts, adequate patient ventilation will occur before the next attempt.

Research Procedure (Intervention group-VL/FIS)
Following induction of general anesthesia and adequate manual ventilation, the anesthesia provider will attempt to successfully intubate the patient utilizing both, a video laryngoscope and a flexible intubation scope. No more than 2 intubation attempts shall be made. If necessary, between intubation attempts, adequate patient ventilation will occur before the next attempt.

For both the control and intervention groups, the anesthesia provider will be given the option to secure the airway via oral pathway (passage) according to clinical judgment. If a patient's airway has not been secured within the two attempts of the respective, allocation treatment, a third attempt will be made utilizing another technique or device (as a rescue attempt) at the discretion of the anesthesia provider. At this point, no further study data will be collected, except of what device was used for the rescue attempt and any potential Adverse Events.

5.3 Measurements

Morphometric characteristics and airway assessments of all patients will be recorded in the preoperative holding area. Patients will be asked questions to assess degree of irritation. Baseline measures of blood pressure, pulse, oxygen saturation, and End-Tidal CO_2 will be recorded prior to induction. Vital signs will be recorded during preoxygenation, before induction of anesthesia, after induction of anesthesia, during laryngoscopy and/or bronchoscopy, after successful intubation, and 3 times while in recovery (at PACU arrival, at 30 and 60 minutes after PACU arrival). Lastly, we will ask the same questions to the patients about degree of irritation when they're fully awake. Additionally, the anesthesiologist will provide a personal, subjective assessment following successful or failed/rescue intubation with the corresponding research procedure/technique.

Intubation technique: Although the time required for successful intubation is not a primary endpoint for the study, the time and number of attempts required for successful tracheal intubation will be recorded for each patient. The glottis view obtained will be recorded using the percentage of glottis opening (POGO) score. If the epiglottis is down folded and a jaw lift is required to improve view, this information will be reported. The view both before and after jaw lift will also be recorded using the POGO score. If blood or secretions are present and require suctioning, time will be stopped while suctioning occurs and this will be recorded. If rotation of the ETT to obtain intubation is required or esophageal intubation occurs, this will also be recorded. The subjective level of difficulty in the performance of intubation will also be recorded.[2]

Intubation: We will record how long in seconds and number of attempts required for successful endotracheal intubation in each group. An attempt is defined as an attempt at placement of an ETT through the glottic opening, pass the vocal cords, and into the trachea. Removal/reinsertion of the laryngoscope/fiberoptic scope will constitute as a new attempt. If more than 2 attempts are needed or if the anesthesia provider discontinues protocol procedures, for any reason, the case will be deemed a failure.

5.4 Outcomes definitions

Degree of difficulty: Difficult ETT placement is the primary outcome defined as: (i.) either first intubation time >60 seconds or (ii.) first attempt failure at intubation or (iii.) ease of intubation reported as difficult by the provider dichotomized by a scale score of 4 or 5 versus 1, 2, or 3.

Control group-FIS placement: A successful attempt will be defined as when the insertion tip of the FIS enters the patient's mouth (or nose), leading to placement of the ETT into the trachea and confirmation of the end-tidal CO_2 capnography waveform. Any other manipulation of the airway leading to incorrect placement of the ETT will be considered a failed attempt.

Intervention group-VL/FIS placement: A successful attempt will be defined as when the tip of the video laryngoscope blade and insertion tip of the FIS enters the patient's mouth, leading to placement of the ETT into the trachea and confirmation of the end-tidal CO_2 capnography waveform. Any other manipulation of the airway leading to incorrect placement of the ETT will be considered a failed attempt.

Difficult intubation: The subjective level of difficult ETT insertion termed "Ease of Intubation" measured on a Likert scale from 1 to 5, with 1 being "Extremely Easy" and 5 being "Extremely Difficult."

Ease of ETT insertion: The subjective level of ease of ETT passage thought glottis (from 1 = *Extremely Easy* to 5 = *Unsuccessful*) in the performance of the randomized intubation technique (FIS vs VL/FIS) will be recorded.

Incidence of desaturation: Incidence of oxygen saturation $\leq$92% will be recorded.

Degree of Irritation: The subjective level of irritation provided by the patient (*0 = None; 1= Mild; 2 = Moderate; 3 = Severe*) perioperatively (both pre and post operatively) will be recorded.

Total Time: The total time from the beginning of either FIS or FIS/VL combination insertion until successful ETT intubation in seconds, as verified by capnographic waves, chest rise and fall, and fogging of the ETT will be recorded.

Total Score: Outcomes for each of the 3 items: i) time of intubation, ii) number of attempts, and iii) the number of complications, a total score will be derived for each patient. Each outcome will be translated into a binary scale. For example, starting with intubation time, the completion a procedure within 60 seconds will be assigned a '0', and completion taking more than 60 seconds will assign a '1'. For the number of attempts, we will assign a '0' for a single attempt and a '1' for more than a single attempt. And finally for complications, we will assign a '0' for no complication arising and a '1' for any complications arising. The total score will range from 0 to 3.

6.0 SUBJECT WITHDRAWALS

Subjects may be withdrawn from the study for the following reasons:

1) Subject non-compliance with study procedures
2) Unacceptable adverse events (safety or tolerability)
3) The subject may withdraw from the study at any time and for any reason
4) Clinician decision that it is in the best interest of the subject to withdraw from the study

7.0 SAFETY AND REPORTABLE EVENTS

7.1 Adverse Event Definition

There is no additional risk as compared to standard risk with this equipment.

7.2 Non-Serious Adverse Event

- Dental damage
- Corneal Abrasion

7.3 Recording Adverse Events

All adverse events, whether observed by the Investigator, elicited from or volunteered by the subject, should be documented. Each adverse event will include a brief description of the experience, the date of onset, the date of resolution, the duration and type of experience, the severity, the relationship to investigational product (i.e., drug or device), contributing factors, and any action taken with respect to the study drug/device.

Investigators and research coordinators will be instructed that all AE and corresponding relevant information should be recorded on the Adverse Event Form. The Principal Investigator will be responsible for reporting AEs to the IRB of record in accordance with IRB procedures.

7.4 Responsibilities for Reporting Serious Adverse Events

The Principal Investigator will record all serious adverse experiences that occur during the study period in the appropriate source documents and/or AE log as applicable.

8.0 RISK/BENEFIT ASSESSMENT

8.1 Potential Risks

There are no additional risks to the standard risk associated with intubation with this equipment.

8.2 Protection Against Risks

Standard protocol will be followed, eye protection after induction of anesthesia; careful placement of equipment to prevent dental damage.

8.3 Potential Benefits to Subjects

- Improved oxygen delivery, administration, and oxygenation
- Improve efficiency of tracheal intubation
- Reduce post-op respiratory complications

8.4 Alternatives to Participation

Standard airway management procedures will be implemented.

9.0 CONFIDENTIALIATY OF DATA AND INFORMATION STORAGE

9.1 Institutional Review Board (IRB)

Prior to participating in this investigation, the site will be required to obtain approval from its governing IRB. The Principal Investigator is responsible for obtaining and maintaining IRB approval to participate in this investigation. The IRB for this study is the institutional IRB at the University of Texas MD Anderson Cancer Center in Houston.

9.2 Subject Data Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Patient data retrieved from the Case Report Forms (CRF's) or patients' electronic medical record will be entered into an online database (i.e. REDCap). PI will consider all information concerning a subject or their participation in this investigation as confidential. Only authorized study personnel will have access to these confidential files and have the right to inspect and copy all of the records pertinent to this study for data verification. This may include medical information gathered prior to the onset of the study. All data used in the analysis and reporting of this investigation will be conducted without identifiable reference to specific subject name. The site will maintain a list matching each subject's name with the study identification in OnCore.

To ensure compliance with the Health Insurance Portability and Accountability Act (HIPAA), all subjects enrolled in the study will be required to provide authorization to disclose Protected Health Information (PHI). This authorization will be included in the informed consent document as required by the IRB. In all study reports and in any resulting publications, their initials and/or study identification will not refer to the subjects.

10.0 SAMPLE SIZE DETERMINATION AND DATA ANALYSIS

10.1 Sample Size Determination

A total of 60 evaluable patients will be randomized to each intervention arm. With 60 patients per study arm, a 2-sided chi-square test with alpha = 0.05, and an assumed rate of difficult ETT in one

arm of 30% on the control arm, then a minimum detectable difficult ETT rate of 10% (an absolute difference of 20 percentage points) would be considered statistically significant (nQuery v7) with power of 80%. For each study arm consisting of 60 patients, estimated rates of difficult ETT will be provided using exact 95% CI using the method of Clopper-Pearson. For example, a rate of 25% would provide exact 95% confidence interval limits that do not exceed (0.15 0.38), exact 99% CI limits that do not exceed (0.12, 0.42) using the method of Clopper-Pearson.

In the pursuit of ensuring that a sufficient number of evaluable patients have been enrolled, an adjustment will be made to the total number of randomized patients by adding 20% or an additional 24 patients (12 per study arm). This modification will result in a total sample size of 144 patients. However, the accrual of participants will cease once 60 evaluable patients have been reached on each study arm.

10.2 Planned Statistical Analysis

For the Secondary Objective:
To evaluate ease of use, each of the 3 dimensions described below will be assessed independently. First, the time of intubation will be assessed for distributional assumptions using histograms, stem and leaf plots, and box plots. Descriptive statistics such as the median and range or the geometric mean ± SD will be used to summarize the data. Second, ordinal data describing the number of attempts will be summarized using the median and range; and third, the number of complications will be summarized using the median and range. For number attempts and complications, frequencies and percentages will be used if the maximum number is small ($\leq$ 4 attempts or complications). Comparisons between continuous covariates of interest will be conducted using a t-test, or Wilcoxon rank-sum test if more appropriate. Categorical covariates will be compared using chi-square or Fisher's exact test.

10.3 Exploratory Analyses

Depending on the distributional assessment of outcomes for each of the 3 items: i) time of intubation, ii) number of attempts, and iii) the number of complications, a total score will be derived for each patient. Each outcome will be translated into a binary scale. For example, starting with intubation time, the completion a procedure within 60 seconds will be assigned a '0', and completion taking more than 60 seconds will assign a '1'. For the number of attempts, we will assign a '0' for a single attempt and a '1' for more than a single attempt. And finally for complications, we will assign a '0' for no complication arising and a '1' for any complications arising. The total score will range from 0 to 3 and will be summarized using frequencies and percentages related to each level of the total score and using the mean score and standard deviation, whichever is more appropriate. Other exploratory outcomes include: Ease of ETT insertion (ranked on a 1 to 5 scale as described in Section 5.4) and will be summarized using descriptive statistics. These exploratory study outcomes will be compared between treatment arms using an independent samples t-tests or chi-square tests. Potential cut-points for these exploratory outcomes may be considered to inform if low versus high scores are associated with select patient outcomes of interest. Cumulative incidence plots will be used to visualize time to intubation, if appropriate. Multiple logistic regression analyses will be conducted to assess the association between any dichotomous outcomes of interest and type of intervention after adjusting for select covariates of interest.

11.0 DATA MONITORING

All randomized studies conducted at MDACC are required to have a DSMB, unless noted otherwise.

11.1 Training of Clinical Site Personnel

The training of clinical site personnel will be the responsibility of the PI. To ensure uniform data collection and protocol compliance, fully delegated study staff will review the investigational plan, techniques for the identification of eligible subjects, instructions on data collection, methods for soliciting data from alternate sources, and schedules for follow-up, as necessary, with the research coordinators.

11.2 Data Reporting

All data will be recorded on the site's standard source documentation. The Investigator or designee is responsible for transferring the information to the appropriate Case Report Forms (CRFs) supplied by the Investigator. The Investigator is responsible for ensuring the forms are accurately completed at the time of, or as soon as possible after, the subject procedure or the availability of test results. The Investigator is required to sign the CRF on the appropriate page(s) to attest she has reviewed the recorded data.

11.3 Data Review

The PI will review all CRFs for completeness and clarity upon receipt. Missing or unclear data will be requested as necessary throughout the study. The PI will request further documentation, such as physician procedure notes when UADEs and/or malfunctions are observed and reported. The Principal Investigator will permit inspection of the study files and subject CRFs by IRB representatives and/or responsible government agencies.

11.4 Data Management

All of the study data will be collected on a paper case report form (CRF), which will be entered in a computer database. Each subject will be registered in OnCore and assigned a sequential number code. The key linking the code and the subject identifier will be kept in OnCore. The computer database will be password protected. All changes to the CRF will follow Good Clinical Practice guidelines. The Research Manager is responsible for auditing the consistency of the data transcribed from the paper CRF to the computer. A protocol violation log will be maintained, and all protocol violations will be reported to the IRB.

12.0 INVESTIGATOR REPORTS AND RESPONSIBILITIES

Investigators are responsible for ensuring the investigation is conducted in accordance with the study protocol and applicable Federal regulations (21 CFR, Part 812, Subpart E). Investigators are also responsible for:

- Obtaining IRB approval for study conduct and re-approval as applicable (if more than one Investigator is participating in the study at a site, the Principal Investigator shall be responsible for the IRB approval and re-approvals)
- Obtaining informed consent of study subjects prior to enrollment into the clinical study
- Protecting the subject rights, safety, and welfare
- Maintenance of subject records and confidentiality
- Record retention as defined in Federal regulations 21 CFR, Part 812.140 (a), (d), and (e)

- Management of investigation and study related activities according to the Clinical Investigator Agreement and the Study Research Agreement
- Submission of site-specific study closure report to governing IRB within 3 months of notification from study Sponsor (if more than one Investigator is conducting the study, the Primary Investigator is responsible for submission of the study closure report)

In addition:

- An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the Investigator's part of an investigation
- If an Investigator uses a device without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing IRB within 5 working days after the use occurs
- An Investigator shall, upon request by a reviewing IRB or regulatory agency official, provide accurate, complete, and current information about any aspect of the investigation

13.0 TIMELINE FOR THE PROPOSED RESEARCH

The timeline to completion of this study will be 12-72 months following IRB approval.

14.0 REFERENCES

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