

Voice Analysis as a predictor for
difficult intubations
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INVESTIGATOR STUDY PLAN - REQUIRED

1. TITLE

Voice Analysis as a predictor for difficult intubations

2. EXTERNAL IRB REVIEW HISTORY*

N/A – no external IRB review.

Principal Investigator: J. Matthias Walz, MD

3. PRIOR APPROVALS:

Conflict of Interest (COI):

N/A

Clinical Engineering Department:

Not applicable.

Biohazardous Agents:

N/A

4. OBJECTIVES*

Purpose:

To investigate if signal processing can detect subtle changes in speech production clinically relevant to oropharynx anatomy that may provide an objective measure in the assessment of the presumed difficulty of intubation.

Specific Aims:

1. Develop an algorithm, using signal processing to detect subtle changes in the production of syllables to evaluate oropharynx anatomy in order to predict difficulty in intubation.
2. Use the algorithm in a prospective cohort trial to predict difficult intubations.

Objectives:

1. The primary objective of this study is to develop a speech analysis algorithm that will provide an objective measure of the difficulty of an airway to undergo safe intubation.
2. The secondary objective is to use this algorithm in a prospective trial to predict difficult oropharyngeal anatomy.

Hypothesis:

Changes in phonation can be used as a reliable measure for the prediction of difficult to manage airways.

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5. BACKGROUND*

Current practice for preoperative anesthesia workup uses a variety of subjective measures to determine the presumed difficulty of managing an airway. With the most efficacious measure of a difficult airway being prior difficulty in intubation, it leaves a large group of patients without an objective measure of difficulty. Preoperative assessments of patients have several markers of a difficult airway but none have proven to be both highly sensitive and specific, furthermore each of these markers are highly subjective, further confounding of the assessment. While no similar study could be found after an exhaustive literature search the building blocks for this analysis have already been performed. Multiple studies have shown that specific characteristics of the speech can correlate with oropharynx anatomy that correlate to a disease state. Prior research has shown that analysis of vowel production specific to velar vowels can be used to predict obstructive sleep apnea which is a disease state associated with difficult ventilation. We believe that similar analysis can be used as an objective measure to predict a difficult airway. Given that there is a large population of patients who have never undergone anesthesia we lose the only sensitive and specific marker of a difficult airway. Given the inherent risk of an uncontrolled airway we feel that it is in our patient's best interest to focus on objective measures to aid in the prediction of a difficult airway. Development of a simple voice analysis algorithm that has the ability to objectively predict a difficult airway could revolutionize preoperative analysis of patients and provide them with safer anesthesia.

Reference:

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6. D, J. A. Fiz, J. A., Morera, J., Abad, J., Belsunes, A., Haro, M., & Jane, R. Acoustic analysis of vowel emission in obstructive sleep apnea. *Chest* 1993 104: 4; 1093-1096

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7. Robb, M. P., Yates, J., & Morgan, E. J.. Vocal tract resonance characteristics of adults with obstructive sleep apnea. *Acta Oto-Laryngologica*. 1997; 117; 760-763
8. Arthur W Fox M D, F. C. C. P., D, P. K. M. P., & C Duane Morgan M D, F. C. C. P. Speech Dysfunction of Obstructive Sleep Apnea. *Chest*, 2006 96(3), 589–595

6. INCLUSION AND EXCLUSION CRITERIA*

Phase 1:

Inclusion Criteria

1. 18 years of age or older
2. Able to provide informed consent
3. A known documented history of having a difficult airway
4. An age-matched control subject with normal airways.

Exclusion Criteria

1. Unable to consent for themselves
2. Non-English speaking subjects
3. Pregnant Subjects
4. Previous Vocal Cord Surgery
5. Previous Head and neck surgery that would alter anatomy of hypopharynx

Phase 2:

Inclusion Criteria

1. 18 years of age or older,
2. Able to provide informed consent

Exclusion Criteria

1. Unable to consent for themselves,
2. Non-English speaking subjects,
3. Pregnant Subjects.
4. Previous Vocal Cord Surgery
5. Previous Head and neck surgery that would alter anatomy of hypopharynx

We will not include:

- Prisoners
- Pregnant women
- Individuals who are not yet adults (infants, children, teenagers)
- Adults unable to consent
- Adults who cannot speak English

We will not be enrolling subjects who cannot speak English. The subjects must be able to understand the research team member who is testing them.

7. STUDY-WIDE NUMBER OF SUBJECTS*

N/A

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8. STUDY-WIDE RECRUITMENT METHODS*

N/A

9. STUDY TIMELINES*

The duration of the subject's participation will be less than 15 minutes while in the Pre Surgical Evaluation clinic or outpatient clinic room where they will be asked to record several small speech segments into a microphone. A medical record review will be performed after the subject's surgical procedure.

We anticipate that it will require approximately 2 years to enroll all study subjects into Phase 1 and Phase 2 of the research study. Chart reviews are expected to be performed for approximately 1 year after enrollment of the last subject.

The estimated period of time required to complete this study will be approximately three years.

10. STUDY ENDPOINTS*

Primary endpoints:

Is speech analysis more specific and sensitive than current airway analysis techniques?

11. PROCEDURES INVOLVED*

The study will be conducted in 2 Phases. Subjects enrolled into Phase 1 will not be enrolled into Phase 2.

Phase 1:

Phase 1 will consist of enrolling 25 subjects with a documented history of difficult airways and 25 subjects of the same age (matched for age) with normal airways to be used as controls. There is a chart of approximately 150 patients with documented difficult airways held by the Dept. of Anesthesia. When the patient was labeled as a difficult airway during their hospitalization, they were given a copy of the difficult airway documentation so the patient should be aware already that they are labeled as a difficult airway. There will be a chart review done to determine if the patients are still alive and eligible for Phase 1 of this study. If they are eligible, a member of the research team will contact the patient over the telephone to ask if they would be interested in participating in Phase 1 of the study. The location for the visit will be coordinated and they will be given parking validation for the visit.

1. Confirm eligibility over the telephone in the PSE clinic or outpatient clinic room
2. The subject will sign the informed consent and HIPAA forms
3. The subject will be asked to say several syllables into a digital microphone that is attached to a laptop. The subject's voice recordings will be saved in a FLAC audio file. FLAC audio files will be chosen because there is no compression of the audio file making it the highest quality data that can be acquired. The recordings will be labeled with the subject's study ID number only.
4. If applicable, a medical record review will be performed after the subject has undergone their surgical procedure to collect information required for the study. Once the subject is discharged from the hospital we will access their medical record to review their anesthesia experience.

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Phase 2:

Phase 2 will consist of 500 subjects

1. Confirm eligibility in the PSE clinic
2. The subject will sign the informed consent and HIPAA forms
3. The subject will be asked to say several syllables into a microphone. The recordings will be labeled with their study ID number only.
4. A medical record review will be performed after the subject has undergone their surgical procedure to collect information required for the study. Once the subject is discharged from the hospital we will access their medical record to review their anesthesia experience.

12. DATA AND SPECIMEN BANKING*

N/A

13. DATA ANALYSIS and MANAGEMENT*

Statistical Analysis

$$N = \frac{p_0 q_0 \left\{ z_1 - \frac{\alpha}{2} + z_1 - \beta \sqrt{\frac{p_1 q_1}{p_0 q_0}} \right\}^2}{(p_1 - p_0)^2}$$

$$q_0 = 1 - p_0$$

$$q_1 = 1 - p_1$$

p_0 = incidence of difficult airway in population

p_1 = incidence of difficult airway in study group

N = sample size

α = probability of type I error

β = probability of type II error

z – critical Z value for a given α or β

$$N = \frac{0.02 * 0.98 \left\{ 1.96 + 0.84 \sqrt{\frac{0.04 * 0.96}{0.02 * 0.98}} \right\}^2}{(0.04 - 0.02)^2}$$

$$N = 483$$

Current literatures suggest that the incidence of a difficult airway are 1.1-3.8% in the general population, with an accepted gross average of 2%. Given that the study group is has been selected of criteria that put them had higher risk for a difficult airway an incidence of 4% has been used. Using a power analysis shown above a sample size of 500 is supported.

The current data analysis plan will involve sending the audio samples of speech production with all identifying data stripped to a blinded analyst. Each sample will be broken down into its signal components using signal-processing methods. The results of the signal processing will be the

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used to predict a difficult airway. Using these predictions we will then correlate with each subjects clinical outcome to verify the predictive value of speech analysis.

Quality control procedures will all be in the form of data collection to ensure the highest quality of data acquisition.

The Data Collection sheet will be filled out before and during each session.

14. PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS*

Minimal Risk

15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT*

Subjects may be withdrawn if the study is discontinued.

16. RISKS TO SUBJECTS*

Risk of Confidentiality

Efforts will be made to limit access to the subject's personal information, including research study information and medical records, to people who have a need to review this information. UMMS Institutional Review Board and other representatives of UMMS may need to review records of individual subjects. As a result, they may see their name, but they are bound by rules of confidentiality not to reveal the subject's identity to others. There is a risk of breach of confidentiality.

17. POTENTIAL DIRECT BENEFITS TO SUBJECTS*

Subject will not benefit directly from being in this research study.

18. VULNERABLE POPULATIONS*

N/A We will not be enrolling pregnant women, adults lacking capacity, children younger than 18 years of age or prisoners.

19. MULTI-SITE RESEARCH* N/A

20. COMMUNITY-BASED PARTICIPATORY RESEARCH* N/A

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*

Subjects will not receive any study results.

22. SETTING

Facilities: The research will take place at UMass Memorial Medical Center at the Pre-Surgical Evaluation Clinic (PSE) at the Memorial campus or an outpatient clinic room at University Campus. The area has access to the electronic charting system (outpatient clinics and/or inpatient hospital areas) allowing access to the research subject's data required by the study.

Identify potential subjects

HIPAA waiver is necessary for screening purposes. Subjects must have a documented history of a difficult airway. The matching control must be the same age. We are hoping to enroll into the Phase 1 arm of the study quickly so that Phase 2 can be initiated. Rather than putting subjects

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through the undue stress of getting information for a research study that they may not even qualify for, we would like to approach those who meet eligibility criteria only. This plan makes it impracticable to ask each subject for access to their records to assess eligibility. The research staff will review the Dept of Anesthesia binder of difficult intubation patients to determine which patients meet criteria. If necessary, the PSE staff will contact the anesthesia research nurse/coordinator with the subject' name and medical record number to screen. We will access the subject's PHI (name, DOB, date of surgery, medical record number, patient status: able to consent for themselves etc) at that time.

Where research procedures will be performed:

Subjects will be seen at the PSE clinic at the Memorial campus or an outpatient clinic room at University Campus.

Composition and Involvement of any community advisory board: N/A

Research conducted outside of the organization and its affiliates:

N/A All recruitment methods will be local and no materials will be used.

23. RESOURCES AVAILABLE

Time that will be devoted to conduct and complete the research: Adequate time has been allocated for enrollment, completion of study procedures and analyzing data. The PI, research, nursing and scientific personnel will work the necessary hours to complete the project. All individuals involved in the conduct, reporting, and/or design of the research will be added to eIRB prior to their involvement.

The staff involved in the research project: This staff consists of physicians, nurse practitioners, research nurses and research coordinators. Collectively the staff has over 20 years of clinical research experience at UMMS. The roles of each research staff member is listed below:

Principal Investigator:

- The PI is a resident in the Department of Anesthesiology & Perioperative Medicine. This position requires training in Anesthesiology and experience with research design and laboratory methods. The PI is responsible for ensuring that all team members have current CITI training, appropriate training for their respective roles, including knowledge of the study protocol and procedures for maintaining confidentiality. The PI may consent subjects, discuss potential subjects with the attending physician, perform the voice analysis, data analysis and perform any other study related procedures that fall within their scope of practice only after receiving the appropriate training required to perform the procedures.

Faculty Advisor

- The Faculty Advisor is a M.D. who will oversee the conduct of the research. As Faculty Advisor, this individual is expected to oversee and train the PI/resident in matters of appropriate research compliance, protection of human subjects and proper conduct of research. The Faculty Advisor is also responsible to assure that the research is conducted in accordance with Institutional Policies

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and Procedures and the Investigator Manual (HRP-910). This position requires advance training in Anesthesiology and/or Neurology. The Faculty Advisor may assist with consenting subjects, collecting data, data analysis and performing any other study related procedures that fall within their scope of practice only after receiving the appropriate training required to perform the procedures.

Sub investigators:

- This position requires advance training in Anesthesiology and/or Neurology. Sub-investigators may be responsible for consenting subjects, collecting data, data analysis and performing any other study related procedures that fall within their scope of practice only after receiving the appropriate training required to perform the procedures.

Research Nurse (Coordinator)

- This position requires a registered nurse with advanced training in the critical care area. Research nurses may be responsible for handling IRB submissions, overseeing regulatory responsibilities, screening and consenting subjects, data analysis and performing any other study related procedures that fall within their scope of practice only after receiving the appropriate training required to perform the procedures. They will have completed all JCAHO required annual competencies to practice in the hospital.

Research Coordinator

- This position requires a specialized research professional working with and under the direction of the Principal Investigator (PI). Research coordinators support, facilitate and coordinate the daily clinical trial activities and play a critical role in the conduct of the study. Their responsibilities include: maintaining records, handling IRB submissions, data management, and performing any other study related procedures that fall within their scope of practice only after receiving the appropriate training required to perform the procedures.

A trained and experienced research coordinator and/or research nurse will perform various tasks required by the study at various time points. A trained and experienced research coordinator and or research nurse will enter subject data into the electronic CRF, and perform regulatory functions required by the study.

Availability of medical or psychological resources: N/A

Process to ensure that all persons assisting with the research are adequately informed about the protocol: All research personnel that are involved in the protocol will be trained by the PI at the initiation visit. If they are unable to attend the initiation visit, the PI or a person they feel is appropriately knowledgeable will provide training including: the flow of the research study, procedures required by the protocol, the researcher's duties and functions. A signature log of all those trained

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will be kept in the Regulatory Binder of the study. The binder is kept in a secure location with minimal access to unauthorized personnel (in the anesthesia research office). The clinical staff caring for the subject will be given information regarding the study.

24. LOCAL RECRUITMENT METHODS

Feasibility of recruiting the required number of suitable patients within the agreed recruitment period: Prior to the start of the study, Dr. Lotz confirmed that our site should be able to recruit the required number of appropriate patients for the study.

Screening:

There is a binder of documented difficult airway patients kept by the Dept of Anesthesia. The chart will be reviewed by research staff for eligible patients. If the patient meets criteria for Phase 1, the subject will be contacted over the telephone to ask if they are interested in participating. If they are interested in participating the research staff will set up an appointment and we will provide parking validation for the patient.

Every individual who attends the Pre-Surgical Evaluation (PSE) clinic evaluated for pre surgical clearance, and to evaluate for any possible concerns that could be foreseen during anesthesia. Subjects screened for the study will be seen at the Pre-Surgical Evaluation Center on the same day as their Pre-Surgical Evaluation visit. Each patient that meets the inclusion criteria will be asked by a clinical staff member if they would like to hear more information about this research study. If they agree, a member of the research team will explain the study to the subject. If the subject is not comfortable discussing their involvement at that time, we will ask if they would like to take a copy of the Informed Consent Form home with them to review. If they agree, we will ask if a member of the research team could call them before they are admitted for their surgical procedure or if they prefer we could talk with them when they come to the hospital for their surgical procedure. If they would rather not participate, the conversation will end. We will look for subjects with a known documented history of having a difficult airway. For each subject enrolled, we will recruit a subject of approximately the same age with no history of having a difficulty airway (trouble in the past having a breathing tube inserted to administer general anesthesia).

“See Consent Process” below for details on obtaining informed consent.

Source of patients: The study will be performed at the Pre Surgical Evaluation (PSE) clinic or an outpatient clinic room at University campus.

If necessary we will screen in PSE clinic where patients are evaluated by an Anesthesia provider and their staff to screen incoming patients for any concerning features that may affect their anesthetic care. This Clinic sees on average 15000 patients a year and with the two-year enrollment time we would only need to recruit 3.33% of patients in order to reach our goal.

Methods used to identify potential patients: See “Screening” above. There will be no advertisements or other recruiting methods.

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Phase 1 patients: Patients will be given a \$25 stipend for participation in the study and parking validation (if necessary).

25. LOCAL NUMBER OF SUBJECTS

The total number of subjects to be accrued locally will be up to 550. Since the study will be short and performed during the initial meeting there will no need to distinguish between the expected to enroll and those screened.

26. CONFIDENTIALITY

Local procedures for maintenance of confidentiality:

The subject's research records will be confidential to the extent possible. In all records, the subject will be identified by a code number and their name will be known only to the researchers. The subject's name will not be used in any reports or publications of this study. The UMMS Institutional Review Board and/or their representatives may inspect the subject's medical records that pertain to this research study. They will not be allowed to copy down any parts of the subject's identifiable information or take any of the subject's identifiable information from our office.

Voice recordings will be stored in a password protected, encrypted laptop. The recordings will be destroyed at the end of the study after the final data analysis has been performed.

Where and how will data be stored locally: The source data will be stored in the Anesthesia research office. The Anesthesia Research office is secured with a keypad lock. The combination is known only to authorized individuals. The electronic data is protected in a database that is password protected and encrypted. Voice recordings will be stored in a password protected, encrypted laptop. The recordings will be destroyed at the end of the study after the final data analysis has been performed.

How long will data or specimens be stored locally:

The study documents must be retained in the files of the responsible investigator until the end of the study. De-identified research records, as well as consent forms/HIPAA Authorizations, will be retained as per HRP-800 INVESTIGATOR GUIDANCE: Investigator Obligations. After that time period, the documents may be destroyed, subject to local regulations (shredded).

Who will have access to the data or specimens stored locally: The research nurses, the investigators, and the IRB.

Who is responsible for receipt or transmission of the data or specimens locally: The research nurses/coordinators and the investigators.

How will data and specimens be transported locally: N/A

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

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A HIPAA waiver of authorization will be used to screen any potential subjects. All subjects have signed an HIPAA Authorization Form which describes the protected health information that will be used and disclosed for research purposes. The subjects will be given information to withdraw the right to use any new information if they feel they do not want to continue in the research study.

Only research personnel involved in the research study and trained to conduct the study related procedures will be involved with the subjects.

28. COMPENSATION FOR RESEARCH-RELATED INJURY

This is a minimal risk study. No compensation will be set aside.

29. ECONOMIC BURDEN TO SUBJECTS

There are no foreseeable economic burdens to subjects

30. CONSENT PROCESS

Where will the consent process take place: The consent process will take place in the clinic room with an area that provides privacy to the subject.

Any waiting period available between informing the prospective subject and obtaining consent: The subject will be given as much time as possible to decide whether they would like to participate in the research study. All questions will be discussed. If the subject is not comfortable making a decision, the subject will not be enrolled.

Any process to ensure ongoing consent: N/A

Informed Consent Process: The principal investigator will ensure that informed consent is obtained in accordance with the SOP: HRP-802 INVESTIGATOR GUIDANCE: Informed Consent." Those obtaining informed consent and HIPAA from the subject will be a sub investigator, research nurse, research nurse manager or research coordinator who has been properly trained by the principal investigator, is knowledgeable about the study and able to answer any questions the potential subject may ask.

After discussing the study in detail (disease process, risks, procedures and availability of alternative treatments [standard of care]) the subject will be given the informed consent form and HIPAA form to review. The subject will be asked if they understand what has been explained. All questions will be discussed. If they are uncomfortable or hesitant about participating in the research, the consent process will be stopped. If the subject is willing to participate in the research, they will sign and date the informed consent form and HIPAA form. The research staff personnel obtaining consent will sign and date the forms where appropriate. A copy of the ICF and HIPAA forms will be given to the subject. The original ICF and HIPAA Authorization will be placed in the regulatory binder for the research study. A copy of the ICF and HIPAA forms will be placed in the subject's medical record.

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A note is placed in the subject's electronic medical record noting the following:

- The date and time that the informed consent form was signed
- Discussion of the study, questions answered
- Subject met all study entry criteria

All subjects will be included in the consenting process.

We will not be enrolling non-English speaking adults into the study.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

We will be following the "HRP-803 INVESTIGATOR GUIDANCE: Documentation of Consent."

32. DRUGS OR DEVICES

N/A