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IRB Minimal Risk Protocol Template

Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at http://intranet.mayo.edu/charlie/irb/

First-time Use: Use this template to describe your study for a new IRB submission.

1. Complete the questions that apply to your study.
2. Save an electronic copy of this protocol for future revisions.
3. When completing your IRBe application, you will be asked to upload this template to the protocol section.

Modification: To modify this template after your study has been approved:

1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
2. Open the saved document and activate "Track Changes".
3. Revise the protocol template to reflect the modification points , save the template to your files
4. Create an IRBe Modification for the study and upload the revised protocol template.

General Study Information

Principal Investigator: Cadman Leggett ~~Kenneth K. Wang~~, MD

Study Title: Electronic Nose Identification of Fasting and Non-fasting Breath Profiles

Protocol version number and date: 9.1~~0~~, August 9, 2022 ~~March 16, 2022October 16, 2019~~

Purpose

Hypothesis: An electronic nose can discern breath profiles between fasting and non-fasting individuals

Aims, purpose, or objectives: In patients undergoing endoscopic procedures, there currently is not a non-invasive process to assess whether the patient presents in a fasting state which is required for moderate sedation or anesthesia-assisted endoscopy. With the increased prevalence of type 2 diabetes and its associated co-morbidity of gastroparesis which causes delayed gastric emptying, this may present retained food in the stomach even in individuals who comply to standard fasting protocols.

In non-fasting individuals, the risk of a sedation related complication such as aspiration increases and often the procedure must be aborted and repeated on another day following more prolonged fasting and medication administration. This adds to increased cost and delay to patient care.

We propose a mechanism by which we can quickly screen and assess for fasting and non-fasting states in individuals scheduled for routine endoscopy by utilizing a non-invasive breath analyzer called an electronic nose by which through pattern recognition we analyze electronic changes in exhaled volatile organic compounds interfacing with an electronic sensor that creates an electronic signature, or smell-print that distinguishes the fasting and non-fasting states.

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc*.): We eNose Company (eNose B.V., Zupten, NL), who will supply the electronic nose apparatus called the Aeonose device. This is a handheld, portable battery operated unit with a built in sensor that allows for data collection at the point of care with the subject breathing directly into the apparatus. The technology which is based on the prior commercially available Diagnose which was CE marked, and the Aeonose has already been utilized in large studies in breath analysis for head and neck cancer screening[1], tuberculosis screening[2], and is nearing commercialization by the eNose Company.

We have demonstrated experience working with the eNose Company in our study Identification of C. difficile infected stool by electronic nose using a device (Aetholab) with the same sensor technology (14-001369).

Preliminary studies show that signal separation can be detected within as few as 50 signals of 25 positive and 25 negative for training. A maturation process of pattern recognition occurs with 200 signals, 100 positive and 100 negative respectively. This is an initial pilot which can be expanded to the scale of a full study pending promising results. As we will be collecting positive and negative signals from the same patients, we anticipate subject numbers half that of the required signal training numbers.

References:

1. Leunis N, Boumans M-L, Kremer B, et al. Application of an electronic nose in the diagnosis of head and neck cancer. *Laryngoscope*. 2013:13-16. doi:10.1002/lary.24463.

2. Bruins M, Rahim Z, Bos A, van de Sande WWJ, Endtz HP, van Belkum A. Diagnosis of active tuberculosis by e-nose analysis of exhaled air. *Tuberculosis (Edinb)*. 2013;93(2):232-8. doi:10.1016/j.tube.2012.10.002.

Subject Information – charts, records, images, or specimens are considered 'subjects'

Target accrual is the proposed number of subjects to be included in your study at your site. "Subjects" may include Mayo Clinic charts, records, or specimens, ***and/or*** *charts, records, or specimens received at Mayo Clinic from external sources for collaborating analysis by the investigator under this IRB application*:

Target accrual: 1000 patients

Subject population: Any outpatient adult individual undergoing elective upper endoscopy who consents to study participation

Inclusion Criteria:

1. English speaking
2. Adult (18+) patient undergoing scheduled elective outpatient upper endoscopy
3. Willing and able to consent to research protocol
4. Fasting as required per routine instruction for endoscopy or non- fasting adults accompanying the patient who are able to provide informed consent
5. Able to breath for approximately 5 minutes pre procedure into the Aeonose device with a nose-plug on

Exclusion Criteria:

1. Non-fasting per protocol, or known to have had food or drink outside of routine protocol
2. Non-English speaking
3. < 18 years of age
4. Unable or unwilling to consent to research protocol
5. Inability to tolerate Aeonose breathing (such as those with claustrophobia, anxiety, nasal trauma, etc.)
6. Use of antibiotics or systemic immunosuppressants within three months prior to the date of endoscopy (intranasal and inhaled steroids are allowed)
7. Any prior chemotherapy for esophageal cancer
8. History of squamous cell carcinoma
9. History of gastric or esophageal surgery
10. Per PI discretion, any current medical problem that could alter intended study data collection.

☐ Yes ☒ No Will a Certificate of Confidentiality (COC) be obtained from NIH? If yes,
Who is obtaining the COC: Mayo Clinic investigator, study sponsor, other:
Explain why a COC is needed:

Study Design

Methods: *Describe, in detail, the research activities that will be conducted under this protocol*:
Fasting individuals undergoing upper endoscopy in the gastroenterology unit or non-fasting adults accompanying the patients will be enrolled for participation in Aeonose pre-procedural breath testing. These include elective inpatient procedures which have high risk of gastric content retention, but also have increased health risks due to active comorbidities.
Individuals consenting to participation of this study will be asked to provide a breath analysis using the Aeonose per standard acquisition protocol which spans 5 minutes of which the individuals breaths normally through a sterile disposable mouthpiece with sterile disposable air filters for 5 minutes during signal acquisition while wearing a nose plug. This may be completed prior to their endoscopic procedure.
The signals generated from each subject consist of a de-identified electronic breath-print will be analyzed by the investigators and the aggregate results matched using pattern recognition techniques to localize into fasting and non-fasting states. For the pilot portion of this study, the primary outcome is to establish separation of these signals in the initial cohort.

Resources: *Describe the available resources to conduct the research (personnel, time, facilities, mentor commitment, etc.)*:

The lab group and study team consists of a full time laboratory researcher, gastroenterology clinical investigator fellows, and clinical research coordinators to support the study. The lab is based in the Alfred Main laboratory space. The lab group has already received on-site training by the eNose Company in the operation of the Aeonose. One Aeonose unit is immediately available for dedicated use towards this project and a sufficient supply of disposables (filters and mouthpieces) is already in stock for this project. The eNose Company who is a collaborating partner has dedicated further resources (more Aeonose units and disposables) as needed.

Check all that apply. If none apply, leave blank:

☐ This is a multisite study involving Mayo Clinic and non-Mayo Clinic sites.
When checked, describe the research procedures/activities being conducted **only** at Mayo Clinic:

☐ Mayo Clinic staff will be engaged in research activity at a non-Mayo Clinic site. *When checked, provide the location and a detailed description of the Mayo Clinic research staff involvement*.

☒ This study is to establish and/or maintain an ongoing database or registry for research purposes only.

☒ The research involves contact or interaction with subjects, for example, surveys, questionnaires, observation, blood draw.

☐ The study involves photographing, audiotaping or videotaping subjects (and guests).

Blood Collection

If this study involves prospective blood collection by finger, heel, ear stick or venipuncture, complete the following:

☐ **From healthy, non pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8 week period and collection may not occur more frequently than 2 times per week.

Volume per blood draw: _____ml

Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.) _____

☐ **From other adults and children considering age, weight, and health of subject.** For a minimal risk application, the amount of blood drawn from these subjects may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period, and collection may not occur more frequently than 2 times per week.

Volume per blood draw: _____ml

Frequency of blood draw (e.g. single draw, time(s) per week, per year, etc.)_____

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Review of Chart, Images, Specimens

Provide the date range for collection of data and/or specimens that will be included in your research dataset. *Example: 01/01/2000 to 12/31/2013* or all records through mm/dd/yyyy.

For a retrospective chart review, enter the date range: All records through date of sample acquisition; to correlate any medication, disease, or breath modifying factors, consent will be obtained to retrospectively review the patient's medical chart for correlation purposes. No identifying information will be used in association with the breath print. The breath print cannot be used to identify an individual.

Check all that apply:

☐ This study involves only data and/or specimens that exist at the time this application is submitted to the IRB (IRB submission date). No data or specimens will be collected beyond this date.

☐ This study involves only data and/or specimens that will be collected after submission to the IRB.

☒ The study involves data and/or specimens that exist at the time of submission to the IRB **and** data and/or specimens that will be collected after submission to the IRB, for example a study that includes collection of existing data and prospective collection of specimens.

☐ Data and/or specimens used in this study are collected under another IRB protocol. *When checked, provide the IRB number(s) from which the research material will be obtained. When appropriate, check the box below to attest that subjects have provided consent for future use of their data and/or specimens, as described in this protocol*.

IRB Number/s - Data Only: _____

IRB Number/s - Specimens Only: _____

IRB Number/s - Data and Specimens: _____

Note: When subjects provided consent for use of their data and/or specimens, as described in this protocol.

☐ Other data sources will be utilized in this study, e.g. receiving data/specimens from an external party. When checked, provide all data sources:


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Data Confidentiality, HIPAA Subject Identifiers

Review the list of subject identifiers below and, if applicable, check the box next to each subject identifier being recorded at the time you are collecting/abstracting data/specimens for use in this study.

Subject Identifiers: Individually identifiable information, including demographic data, that identifies the individual or for which there is reasonable basis to believe it can be used to identify the individual. NOTE: Identifiers apply to subjects enrolled in your study and to the subject's relatives, household members, employers, etc.

Internal refers to subject identifiers that will be included in the dataset maintained by the study team.
External refers to subject identifiers that will be shared with persons outside of the immediate study team, for example, sent to an external collaborator or shared with a national registry.

SUBJECT IDENTIFIERS **Check all that apply**	INTERNAL IDENTIFIER	EXTERNAL IDENTIFIER
Name		
Social Security number		
Medical record/patient registration number, lab accession, specimen or radiologic image number	X	
Study number, subject ID, or any other unique identifying number, characteristic or code that can be used to link the identity of the subject to the data	X	
Dates: All elements of dates [month, day, and year] directly related to an individual. Their birth date, date of death, date of diagnosis, etc. **Note:** Recording a year only is not a unique identifier.	X	
Medical device identifiers and serial numbers		X
Biometric identifiers, including finger and voice prints, full face photographic images and any comparable images		
Web Universal Resource Locators (URLs), Internet Protocol (IP) address numbers, email address		
Street address, city, county, precinct, zip code, and their equivalent geocodes		
Phone or fax numbers		
Account, member, certificate or professional license numbers, health beneficiary numbers		
Vehicle identifiers and serial numbers, including license plate numbers		
If None of the above identifiers will be recorded or maintained in the dataset and/or sent outside of the study team, please check "None".	☐ None	☐ None

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Statistical Information

Note: Power analyses and study endpoints are not needed for a pilot or feasibility studies.

☐ No statistical information. *If checked, please explain*:

Statistical Considerations

Power Statement: This initial portion of the study is a pilot/feasibility study with 25 subjects. Based on the experience of the eNose company who will be providing analytical and statistical support in pattern recognition a minimum of 25 positive and 25 negative samples are needed to start to discern separation. In other models, 100 positive and 100 negative training set is needed to create a robust diagnostic model. Further subjects beyond that, such as in multiple sites further fine tune the diagnostic model through pattern recognition learning algorithms (artificial neural networks).

Sample size calculations using 80% power with a 5% level of significance, assuming a 50% fasting / non-fasting prevalence, with a test with a minimum sensitivity and specificity of 80% suggests that about 450 patients are required to achieve statistical power. We will obtain 200 fasting and 200 non-fasting individuals to achieve aim for an accuracy greater than 85%. An additional blinded test group of 50 fasting and 50 non-fasting subjects will be used for model validation. Statistical modeling for training and validation will be performed by the eNose Company using artificial neural networks for pattern recognition as they have been already providing this support through our research collaboration. We will perform descriptive statistics of patient demographics and characteristics

Data Analysis Plan: The eNose company has proprietary expertise in digital signal processing, artificial neural network pattern recognition techniques, the basis which is on published algorithms and established methodologies. The eNose company in collaboration with the investigators will receive encrypted, de-identified digital signatures for training and create a diagnostic model. If the pilot study proves fruitful, this protocol will be expanded into a full study by increasing the enrollment to a full study.

Endpoints

Primary: To determine the ability of the Aeonose in distinguishing a fasting versus non-fasting breath profile

Secondary: To characterize and study influencing factors on breath analysis that affect the ability of distinguishing a fasting versus non-fasting breath profile