# IRB-HSR PROTOCOL

## Investigator Agreement

BY SIGNING THIS DOCUMENT, THE INVESTIGATOR CONFIRMS:

1. I am not currently debarred by the US FDA from involvement in clinical research studies.
2. I am not involved in any regulatory or misconduct litigation or investigation by the FDA.
3. That if this study involves any funding or resources from an outside source, or if you will be sharing data outside of UVA prior to publication that you will contact the Dean's office regarding the need for a contract and letter of indemnification. If it is determined that either a contract or letter of indemnification is needed, subjects cannot be enrolled until these documents are complete.
4. The proposed research project will be conducted by me or under my close supervision. It will be conducted in accordance with the protocol submitted to and approved by the IRB including any modifications, amendments or addendums submitted and approved by the IRB throughout the life of the protocol.
5. That no personnel will be allowed to work on this protocol until they have completed the IRB-HSR On-line training and the IRB-HSR has been notified.
6. That all personnel working on this protocol will follow all IRB-HSR Policies and Procedures as stated on the IRB-HSR Website http://www.virginia.edu/vprgs/irb/ and on the School of Medicine Clinical Trials Office Website: http://knowledgelink.healthsystem.virginia.edu/intranet/hes/cto/sops/sop_index.cfm
7. I will ensure that all those delegated tasks relating to this study, whether explicitly or implicitly, are capable through expertise, training , experience or credentialing to undertake those tasks.
8. I confirm that the implications of the study have been discussed with all Departments that might be affected by it and have obtained their agreement for the study to take place.
9. That no subjects will be recruited or entered under the protocol until the Investigator has received the signed IRB-HSR Approval form stating the protocol is open to enrollment
10. That any materials used to recruit subjects will be approved by the IRB-HSR prior to use.
11. That all subjects will sign a copy of the most current consent form that has a non-expired IRB-HSR approval stamp.
12. That any modifications of the protocol or consent form will not be initiated without prior written approval from the IRB-HSR, except when necessary to eliminate immediate hazards to the subjects.
13. Any significant findings that become known in the course of the research that might affect the willingness of subjects to enroll or to continue to take part, will be promptly reported to the IRB.
14. I will report immediately to the IRB any unanticipated problems involving risk to subjects or to others including adverse reactions to biologics, drugs or medical devices.
15. That any serious deviation from the protocol will be reported promptly to the Board in writing.
16. That any data breach will be reported to the IRB, the UVa Corporate Compliance and Privacy Office , UVa Police as applicable.
17. That the continuation status report for this protocol will be completed and returned within the time limit stated on the form.

18. That the IRB-HSR office will be notified within 30 days of a change in the Principal Investigator or of the closure of this study.
19. That a new PI will be assigned if the current PI will not be at UVA for an extended period of time. If the current PI is leaving UVa permanently, a new PI will be assigned PRIOR to the departure of the current PI.
20. All study team members will have access to the current protocol and other applicable documents such as the IRB-HSR Application, consent forms and Investigator Brochures.
21. Signed consent forms and other research records will be retained in a confidential manner. Records will be kept at least 6 years after completion of the study.
22. No data/specimens may be taken from UVa without a signed Material Transfer Agreement between OSP/SOM Grants and Contracts Office and the new institution. Original study files are considered institutional records and may not be transferred to another institution. I will notify my department administration regarding where the originals will be kept at UVa. The material transfer agreement will delineate what copies of data, health information and/or specimens may be taken outside of UVa. It will also approve which HIPAA identifiers may be taken outside of UVa with the health information or specimens.
23. If any member of study team leaves UVa, they are STRONGLY ENCOURAGED to use Exit Checklist found on IRB-HSR website at http://www.virginia.edu/provost/facultyexit.pdf.

The IRB reserves the right to terminate this study at any time if, in its opinion, (1) the risks of further experimentation are prohibitive, or (2) the above agreement is breached.

**Investigators Experience**

**INSTRUCTIONS:**
Provide a brief description of the investigators experience in working with this population in the clinical and research arena.
If this study will be done in a foreign country, add their experience working within the foreign country.

Answer/Response:

**Investigators Experience**

**Daniel D. Rowley, MSc, RRT-ACCS, RRT-NPS, RPFT, FAARC** is Clinical Coordinator of Respiratory Therapy Services and he has been working as an adult critical care respiratory therapist for 23-years. He earned a master degree in respiratory care and is credentialed by the National Board for Respiratory Care as a registered respiratory therapist and adult critical care specialist. Patient care experience includes delivering and monitoring respiratory care lung expansion therapy effectiveness among adult patients. He has completed specialized training for adult human subject Electrical Impedance Tomography application and monitoring, as well as formal graduate school education and practical experience in adult human subject clinical research design and study coordination related to respiratory care interventions and outcomes analysis.

**Daniel Gochenour, MSc, RRT-ACCS, RRT-NPS, AE-C** is a Senior Respiratory Therapist and he has been working as an adult critical care respiratory therapist for 4-years. He earned a master degree in respiratory care and is credentialed by the National Board for Respiratory Care as a registered

respiratory therapist and adult critical care specialist. Patient care experience includes delivering and monitoring respiratory care lung expansion therapy effectiveness among adult patients. He has completed specialized training for adult human subject Electrical Impedance Tomography monitoring, as well as formal graduate school education and practical experience as an active sub-investigator with adult human subject clinical research.

**Thomas Malinowski, MSc, RRT, FAARC** is Director of Respiratory Therapy Services and he has been working as a respiratory therapist for over 40-years. He earned a master degree in respiratory care and is credentialed as a registered respiratory therapist by the National Board for Respiratory Care. Patient care experience includes delivering and assessing respiratory care lung expansion therapy effectiveness among adult patients. He has formal graduate school education and practical experience in adult human subject clinical research design and study coordination related to respiratory care interventions and outcomes analysis.

**Ashley (Charles) Bruce, BSRT, RRT-ACCS** is an adult critical care respiratory therapist with greater than 10 years of clinical practice experience.

**Kyle Enfield, MD, MSc** is a board certified pulmonologist and assistant professor of medicine at the University of Virginia Medical Center. He also earned a master degree in epidemiology and is the medical center's assistant epidemiologist. As an attending pulmonologist, Dr. Enfield has experience managing pulmonary care for adult patients, which includes lung expansion therapy interventions and assessment of its clinical effectiveness. Dr. Enfield is an experienced adult human subject clinical researcher in the area of pulmonary medicine with special knowledge of clinical research design, data management, and outcomes analysis.

**Robert Sawyer, MD** is Professor of Surgery and Public Health Sciences at U. VA Medical Center. He is Chief of Acute Care Surgery and a U.S. board certified surgeon with specialty training in adult critical care medicine. Dr. Sawyer has extensive research experience that has resulted in manuscript publications in peer reviewed medical journals.

## Signatures

**Principal Investigator**

| _____ | _____ | _____ |
|---|---|---|
| Principal Investigator Signature | Principal Investigator Name Printed | Date |

The Principal Investigator signature is ONLY required if this is a new protocol, a 5 year update or a modification changing the Principal Investigator.

**Department Chair**

BY SIGNING THIS DOCUMENT THE DEPARTMENT CHAIR AGREES:

1. To work with the investigator and with the board as needed, to maintain compliance with this agreement.
2. That the Principal Investigator is qualified to perform this study.
3. That the protocol is scientifically relevant and sound.

| _____ | _____ | _____ |
|---|---|---|
| Department Chair or Designee<br>Signature | Department Chair or Designee<br>Name Printed | Date |

The person signing as the Department Chair cannot be the Principal Investigator or a sub-investigator on this protocol.
The Department Chair or Designee signature is ONLY required if this is a new protocol or a modification changing the Principal Investigator.

## Brief Summary/Abstract

**INSTRUCTIONS:**
Provide a very brief summary or abstract of this study (500 words or less). Include the purpose or hypothesis, a brief description of the experiment, and plans for data analysis.
DO NOT Reference the sponsors protocol here.
If you plan to deviate from the Sponsor's protocol in any way, such as not doing certain sub-studies, include a description of those deviations in this summary.
For those studies where data will be analyzed collaboratively by multiple sites doing a similar study for which there is no sponsors/common protocol (Collaborative Site Analysis Study) include a description of the common scientific goals/procedures/data points.

Answer/Response:

Pulmonary function is compromised following upper abdominal surgery. The incidence of post-operative pulmonary complications following upper abdominal surgery ranges between 17% and 88%, and it is a common cause of morbidity and mortality. Physicians order Incentive Spirometry (I.S.) and EzPAP® lung expansion therapy following surgery to encourage improved alveolar ventilation and to reduce risks of post-operative pulmonary complications associated with inhomogeneous distribution of ventilation during deep breathing inspiratory efforts. The primary purpose of this study is to determine if there is a difference in regional distribution of ventilation when comparing resting tidal ventilation with Incentive Spirometry (I.S.) and EzPAP® lung expansion therapy in healthy adult human subjects. We are also interested in determining if regional redistribution of ventilation is time dependent. Lung volume areas of interests include ventral, mid-ventral, mid-dorsal, and dorsal regions. Our null hypotheses is that there is no difference.

A convenience sampling of study participants will be invited to participate in our descriptive observational study. Study participants will be randomly allocated to receive I.S. or EzPAP® therapy after informed consent has been obtained. Electrical Impedance Tomography (EIT) monitoring will be used to visualize and measure regional distribution of ventilation during lung expansion therapy.

EIT lung monitoring and descriptive data will be presented as number (%), mean (SD), or median (IQR) as appropriate. To test our primary hypothesis, the difference between continuous level data will be analyzed with one-way multivariate analysis of variance. This is a proof of concept study that will include 30 human subjects. Statistical significance is set at ≤ 0.0125. We have created a password protected SPSS file (SPSS v.23; Chicago, IL) that will be used for this study's data entry codebook and statistical output generator.

## Background

1. **Provide the scientific background, rationale and relevance of this project.**

**INSTRUCTIONS**

- This should include a referenced systematic evidenced-based review when possible.
- If this study involves qualitative research explain the major constructs of your study.

- Do not state in this section what you plan to do in this study. This information should be entered later under "What will be done in this protocol?"
- Do not include the bibliography in this section.
- For studies submitted under the Expedited review criteria, this section need not be more than a few pages.

Answer/Response:

Pulmonary function is compromised following upper abdominal surgery. The incidence of post-operative pulmonary complications following upper abdominal surgery ranges between 17% and 88%, and it is a common cause of morbidity and mortality.

Lung expansion therapy with I.S. is commonly ordered prophylactically in attempt to improve pulmonary function and reduce post-operative pulmonary complications. However, a recent Cochrane Review meta-analysis (do Nascimento, JP et al., 2014) reported no statistically significant difference in post-operative clinical complications when comparing Incentive Spirometry to either no respiratory treatment (RR 0.59, 95% CI 0.30 – 1.18), or to deep breathing exercises (RR 0.67, 95% CI 0.04 – 10.50). The authors rated the GRADE quality of evidence as "Low" and concluded that there is no evidence that Incentive Spirometry is effective in preventing post-operative pulmonary complications following upper abdominal surgery. Further research with improved study design is necessary to determine if I.S. or other forms of lung expansion therapy (EzPAP®) offers any clinical benefit.

Evaluating the effectiveness of lung expansion therapy relies upon global parameter measures such as pulse oximetry oxygen saturation and/or arterial blood gas measurements, chest wall auscultation, and assessment of sputum expectoration following therapy sessions. These global parameters do not provide the sensitivity necessary to evaluate regional lung function responses to therapy, as can be viewed with a chest x-ray or CT image. These diagnostic images provide a static view for regional lung volume assessment. They also rely upon the use of radiation. In our study, we will use Electrical Impedance Tomography (EIT) monitoring to measure regional distribution of ventilation during I.S. and EzPAP® lung expansion therapy to better understand how air travels through ventral, mid-ventrial, mid-dorsal, and dorsal lung regions and to determine if redistribution of lung volume is time dependent. This non-invasive, non-radioactive/non-radiation producing, technology will provide real time quantifiable data that may be used to explore whether there is a difference in preferential regional distribution of ventilation when comparing resting eupneic ventilation to I.S and EzPAP lung expansion therapy We will also evaluate whether there is a difference in regional distribution of ventilation measured immediately after the third lung expansion therapy breathing sequence and post-lung expansion therapy session baseline measurement.

## Hypothesis to be Tested

**INSTRUCTIONS:**
If this study involves biomedical research clearly state the objectives and hypotheses and clearly define the primary and any secondary outcome measures. If this study involves qualitative research clearly state your research hypothesis or question.

This section should not include information already included in other sections such as background information or information from the procedures section.

Answer/Response:
The primary purpose of this study is to determine if there is a significant difference in regional distribution of ventilation when comparing eupneic tidal ventilation to Incentive Spirometry (I.S.) and EzPAP® lung expansion therapy in healthy adult human subjects. Electrical impedance tomography (EIT) will be used to measure regional distribution of ventilation during resting tidal ventilation and during lung expansion therapy.

***PRIMARY RESEARCH QUESTION:***
**Is there a difference in regional redistribution of ventilation when comparing eupneic tidal ventilation during Incentive Spirometry (I.S.) or EzPAP® lung expansion therapy in healthy adult human subjects?**

***Null hypothesis:*** There is no difference in regional redistribution of ventilation when comparing eupneic tidal ventilation during Incentive Spirometry (I.S.) or EzPAP® lung expansion therapy in healthy adult human subjects?

***Alternative hypothesis:*** There is a difference in regional redistribution of ventilation when comparing eupneic tidal ventilation during Incentive Spirometry (I.S.) or EzPAP® lung expansion therapy in healthy adult human subjects?

***SECONDARY RESEARCH QUESTIONS:***
**1. Is there a difference in regional redistribution of ventilation measured immediately after lung expansion therapy when compared to regional distribution of ventilation measured 5-minutes after lung expansion therapy?**

***Null hypothesis:*** There is no difference in regional redistribution of ventilation measured immediately after lung expansion therapy when compared to regional distribution of ventilation measured 5-minutes after lung expansion therapy?

***Alternative hypothesis:*** There is no difference in regional redistribution of ventilation measured immediately after lung expansion therapy when compared to regional distribution of ventilation measured 5-minutes after lung expansion therapy?

## Study Design: Biomedical

**1. Will controls be used?**
Answer/Response: Yes.

**►IF YES, explain the kind of controls to be used.**
Answer/Response: Healthy adult human subjects allocated to receive Incentive Spirometry.

**2. What is the study design?**

Example: case series, case control study, cohort study, randomized control study, single-blind, double-blind, met-analysis, systematic reviews, other. You may also view the IRB-HSR Learning Shot on this topic to help you answer this question. (http://www.virginia.edu/vpr/irb/learningshots/Writing_protocol_June09/player.html

Answer/Response: Randomized controlled proof of concept descriptive observational study.

**3. Does the study involve a placebo?**

Answer/Response: No

**►IF YES, provide a justification for the use of a placebo**

Answer/Response:

## Human Participants

**Ages:** _18 – 79 years___
**Sex:** _Male and Female___
**Race:** _All___

**Subjects- see below**

**INSTRUCTIONS:** For question 1-4 below insert an exact #. Ranges or OPEN is not allowed. This # should be the maximum # you expect to need to enroll (i.e. sign consent) If you are only collecting specimens the number of participants should equate to the # of specimens you need. If you are collecting only data from a chart review the number should designate the number of subjects whose medical records you plan to review. Age/ Sex/Race criteria should designate the demographics of participants from whom you will obtain the specimen/data.

**1. Provide target # of subjects (at all sites) needed to complete protocol.**

**INSTRUCTIONS:** If this is NOT a database protocol, this number should be the same as the number of subjects needed to obtain statistically significant results.

Answer/Response: 30. This is a proof of concept study. No power analysis was performed.

**2. Describe expected rate of screen failure/ dropouts/withdrawals from all sites.**

Answer/Response: No drop out is expected.

**3. How many subjects will be enrolled at all sites?**

**INSTRUCTIONS:** This number must be the same or higher than the # from question # 1 in order to account for the # of screen failures, dropouts, withdrawals described in question # 2.

Answer/Response: 30

**4. How many subjects will sign a consent form under this UVa protocol?**

**INSTRUCTIONS:** If the protocol does not have a consent form- the number listed here should reflect such things as the number of subjects from whom specimens will be obtained, the number of charts to be reviewed etc.

Answer/Response: 30

**5. Provide an estimated time line for the study.**

**INSTRUCTIONS:** This should include timelines for enrollment (e.g 50 % enrolled in one year, 100% enrolled in two years), completion of follow-up (if applicable) and completion of data analysis.

Answer/Response: 100% enrollment within three months.

## Inclusion/Exclusion Criteria

**INSTRUCTIONS:**

- The inclusion and exclusion criteria should be written in bullet format.
- *This item applicable if the study will require consent (verbal or written).* Unless there is a scientific reason for not recruiting a certain type of vulnerable population(e.g. not enrolling fetuses, neonates or children in a study regarding Alzheimer's) list the following vulnerable populations under either Inclusion or Exclusion criteria below: pregnant women, fetuses, neonates, children, prisoners, cognitively impaired, educational or economically disadvantage, non- English speaking subjects .
- If you will not enroll subjects who do not speak English because certain procedures cannot be carried out if the subject does not speak English (e.g. a survey is not validated in other languages) insert the following as an Inclusion Criteria: Willingness and ability to comply with scheduled visits and study procedures.
- If this is a collection of only retrospective* specimens or data, the inclusion criteria must include a start and stop date for when specimens/ data will be collected.
- The stop date must be prior to the version date of this protocol.
- *Retrospective: all specimens are in a lab at the time this protocol is approved by the IRB. All data exists in medical records or records from previous studies at the time this protocol is approved by the IRB.

**1. List the criteria for inclusion**

Answer/Response:

- Human subjects 18 – 79 years of age
- Healthy- not receiving in-patient medical care
- Documentation of written informed consent

**2. List the criteria for exclusion**

Answer/Response:

- Less than 18 or greater than 79 years of age
- Body mass index > 50
- Excessive chest hair

- Inability to obtain written informed consent
- Inability to follow verbal instructions
- Pregnancy-self reported
- Uncontrolled body movements
- Inability to place EIT electrodes and belt in direct contact with skin where they are projected to come into contact
- Active implants (i.e., cardiac pacemaker, implantable cardioverter-defibrillator [ICD]), or when device compatibility is in doubt.)

**3. List any restrictions on use of other drugs or treatments**.
Answer/Response: None

## Statistical Considerations

**1. Is stratification/randomization involved?**
Answer/Response: Yes.

**►IF YES, describe the stratification/ randomization scheme.**

INSTRUCTIONS:
The stratification factors and/or the randomization plan should be identified. If there is no randomization component or important patient characteristics that will be used in treatment allocation or data analysis, a statement to this effect should be included.

Stratification factors: These are pretreatment patient characteristics which could be balanced across treatment arms by design or may be used to determine starting dose or treatment allocation.

If randomization is going to be used, the details of the randomization plan should be described.

The description should include:
--the method and timing of randomization
--the type of randomization scheme that will be used in the study
--whether or not the randomization masked/blinded/if so, then to whom is it masked/blinded
--who has access to the randomization scheme

Answer/Response: Parallel randomized controlled trial

A recruitment email will be will be sent to University of Virginia Medical Center employees who represent the target study population. A university of Virginia email distribution list will be used to mass email respiratory therapy and nursing staff working in adult ICU and surgical acute care patient wards. Word of mouth will also be used to heighten awareness about this study. Adult intensive care fellows will also be invited to participate.

The target population will be encouraged to notify a study investigator if they are interested in being screened for eligibility to participate in this study. The study PI and sub-investigators will be responsible for recruitment and enrollment.

A computer generated random numbers generator will be used to randomly assign study subjects into an I.S. or EzPAP® lung expansion therapy group after documentation of informed consent has been recorded. Randomization masking/blinding will not occur in this study. The lung expansion therapy medical device designs and their respective operational differences are impossible to conceal (See images below).

**Lung Expansion Therapy Devices**

**Incentive Spirometer**

**EzPAP® System**

**►IF YES, who will generate the randomization scheme?**

_____ Sponsor
_____ UVa Statistician. Insert name Answer/Response:
_____ UVa Investigational Drug Service (IDS)
__X__ Other: Specify Answer/Response: Study investigators.

**2. What are the statistical considerations for the protocol?**

The objectives section and the statistical section should correspond, and any objective for which analysis is unfeasible should be deleted. Also, the estimates and non-statistical assumptions of the statistical section should be supported by discussion in the background section.

The answer to this question should include:
--Study Design/Endpoints
--Recap of study objectives and endpoint definitions. An assessment of how study objectives will be assessed by identifying & defining which endpoints will be used to assess each component of the study objectives.
--The study design should include contingencies for early stopping, interim analyses, stratification factors (If applicable), and any characteristics to be incorporated in analyses.
--The power/precision of the study to address the major study endpoint(s), the assumptions involved in the determination of power/precision.

--If statistical hypothesis testing is included then specify the null and alternative hypotheses, the test statistic, and the type I and II error rates
--If precision of an estimate, then provide a definition for precision
--If other, then specify

Answer/Response:

The focus of this study is to use electrical impedance tomography (EIT) monitoring to determine if there is a difference in regional distribution of ventilation when comparing Incentive Spirometry (I.S.) to EzPAP® lung expansion therapy.
Baseline characteristics will be reported as:

- Sex (M/F): n (%)
- Age (years): m (SD)
- Weight (BMI): m (SD) or M (IQR) depending upon normality of data distribution
- Tobacco History: n (%); Never smoked, Current smoker; Former smoker
- Respiratory Related Comorbidities: n (%)

Baseline and post-lung expansion therapy dependent variable metrics will be reported as end-expiratory lung volume impedance (EELI) for each of the following ventilation regions of interest:

- Ventral (Level of measurement- continuous)
- Mid-ventral (Level of measurement- continuous)
- Mid-dorsal (Level of measurement- continuous)
- Dorsal (Level of measurement- continuous)

**3. Provide a justification for the sample size used in this protocol.**

Include the anticipated accrual rate, the accrual goal for the study, including accrual goals by strata if appropriate, adjustments for drop-outs etc. and study duration.

Answer/Response: Since this is a proof of concept study, we did not perform a power analysis to determine a sample size.

**4. What is your plan for primary variable analysis?**

Include a sketch of the analysis to assess primary study objectives.

Answer/Response:

***PRIMARY NULL HYPOTHESIS:***
There is no difference in regional distribution of ventilation when comparing Incentive Spirometry (I.S.) lung expansion therapy to EzPAP® lung expansion therapy in healthy adult human subjects

***Alternative hypothesis:*** There is a difference in regional distribution of ventilation when comparing Incentive Spirometry (I.S.) lung expansion therapy to EzPAP® lung expansion therapy in healthy adult human subjects?

- Independent variable
  - Lung expansion therapy
    1. Incentive Spirometry

2. EzPAP®

- Dependent variables
  - Regional distribution of ventilation areas of interest
    1. Ventral end-expiratory lung volume impedance
    2. Mid-ventral end-expiratory lung volume impedance
    3 Mid-dorsal end-expiratory lung volume impedance
    4. Dorsal end-expiratory lung volume impedance

- Statistical analysis
  - Frequency (n) and percentage (%) will be used to report descriptive categorical level data.
  - Shapiro-Wilk test of normality will be applied to evaluate distribution of continuous level data. Normally distributed data will be presented as mean and standard deviation and 95% confidence interval. Effect size will be reported as Cohen's *d.*
  - Non-normally distributed data will be reported as median and interquartile range. Effect size will reported as *r*.
  - Independent samples t-test will be applied to normally distributed continuous data to compare group means, and Mann Whitney-U test will be applied to non-normally distributed data.
  - Statistical significance set a P (2-tailed) ≤ .0125 to reduce risk of Type I error.

**5. What is your plan for secondary variable analysis?**

| Include the following:<br>--A sketch of the analysis to assess secondary study objectives.<br>--For phase III studies, the power/precision of the study to address the secondary objective(s). |
|---|

Answer/Response: Same as above

**6. Have you been working with a statistician in designing this protocol?**
Answer/Response: Yes.

**IF YES, what is their name?**
Answer/Response: Mark Smolkin, University of Virginia Sr. Biostatistician

**7. Will data from multiple sites be combined during analysis?**
Answer/Response: No

| INSTRUCTIONS: IF YES, answer the following questions |
|---|

**7(a). Does the study involve randomization?**
Answer/Response:

**IF YES, will randomization be done at each site or among sites?**
Answer/Response:

**7(b). Has the sample size calculation considered the variation among sites?**

Answer/Response:

**7(c). When combining the data from multiple sites to assess the study results, is the effect of the treatment to be tested (or the association to be tested) assumed to be the same across sites or vary among sites? What is the modelling strategy?**

Answer/Response:

**7(d). Is there a common protocol used in all sites?**

Answer/Response:

**IF NO, how will differences among sites, such as those related to the implementation, inclusion criteria, patient characteristics, or other sites characteristics, be considered to assess the study results?**

Answer/Response:

## Biomedical Research

**1. What will be done in this protocol?**

**INSTRUCTIONS:**
This should include everything that will be done as part of this protocol. Do not repeat information that is included in other sections such as Background or Hypothesis sections. This section should include an indication of which research interventions if any offer a prospect for direct benefit and which interventions (invasive measurements, collection of blood, tissue, data, surveys, etc.) are being done solely to answer a research question and generate generalizable knowledge. If the interventions done solely for research purposes are associated with greater than minimal risk they need to be justified. Describe and justify any control and experimental arm and include method, dose, and duration of drug administration. Reference any claim of clinical equipoise if applicable.

If you are obtaining specimens or data, provide information regarding the type of specimen/data, amount of specimen needed and how the specimen/data will be obtained and what analysis will be done with the specimen/data.

Special note for studies with waiver of consent/waiver of documentation of consent:
Include a statement regarding how subjects will be recruited. For other studies this information is captured in Recruitment does not need to be duplicated in this section.

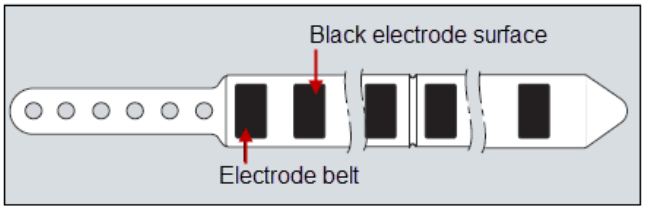
Answer/Response: We will use a convenience sampling scheme to identify potential study participants. Documentation of informed consent will be recorded. Electrical Impedance Tomography (Pulmovista 500; Draeger, Lubeck, Germany), which provides non-invasive and radiation free monitoring, will be used to monitor and measure regional distribution of ventilation during I.S and EzPAP® lung expansion therapy. The PulmoVista 500 EIT device has a reported high patient safety profile and poses minimal patient risk. All study procedures will take place at University of Virginia Medical Center, Second Floor, Pulmonary Diagnostics & Respiratory Therapy Services, Room 2025.

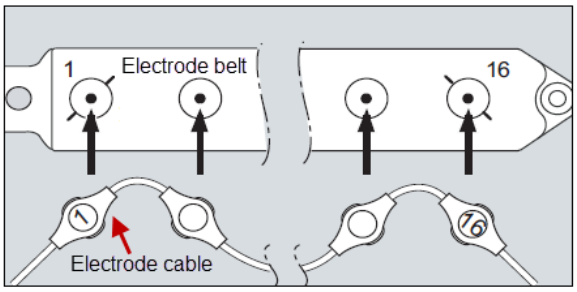
Procedure set-up and device calibration will occur according to Draeger provided PulmoVista 500 (Draeger; Lubeck, Germany) EIT training and operation manual:

- Study participant preparation
  - Researcher will select an electrode belt and respective patient cable sizes after measuring participant's chest circumference with paper measurement tape placed across the midclavicular line at intercostal space 4 -5. Electrode belt size will be selected according to the following chest circumference measurements:

| Chest circumference | Color | Size |
|---|---|---|
| 70 to 85 cm (28 to 33 in) | Medium blue | S |
| 80 to 96 cm (31 to 38 in) | Dark blue | M |
| 92 to 110 cm (36 to 43 in) | Dark red | L |
| 106 to 127 cm (42 to 50 in) | Gray | XL |
| 124 to 150 cm (49 to 59 in) | Violet | XXL |

  - A patient cable of the same electrode belt size will be selected and connected to the electrode belt before connection to study participants. Researchers will align and snap connect the patient cable snaps over the electrode belt studs by aligning respective snaps and studs in ascending numerical order from 1 to 16 (see below).

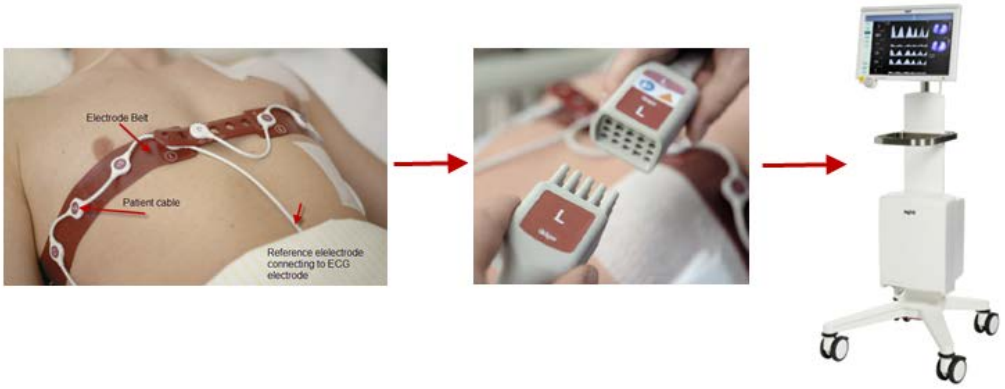


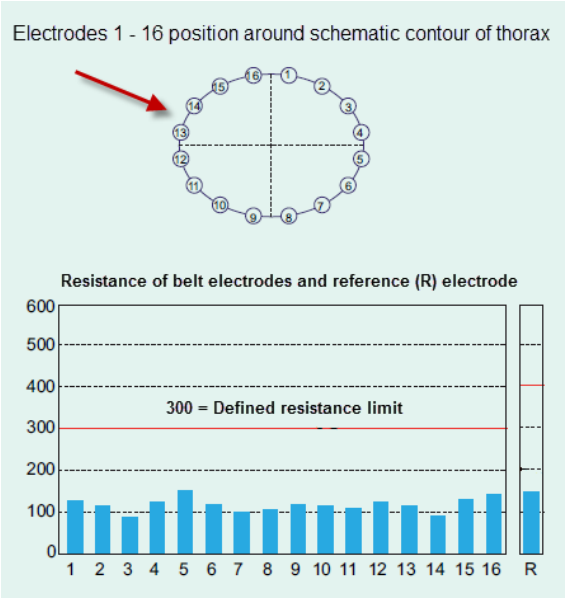

  - A light spray of warm tap water will be applied to the electrode surface on the electrode belt before it is applied to study participants to optimize conductivity between the skin and electrodes.

- Attaching electrode belt and reference electrode to study participant while they are positioned at 45-degrees sitting in a reclining chair.
  - The electrode belt/cable combination will be attached around the thorax of each study participant at the level of the $4^{th}$ – $5^{th}$ intercostal space, unless mammary tissue prevents this site of application. An alternative application site will be located immediately below the mammary tissue if necessary. Left to right belt orientation will be maintained with color coded patient cable ports signifying left and right side (See image).
  - A researcher will snap the electrode belt closed after verifying proper belt position. The belt's black electrodes should have close contact with the study participant's skin at this point.

- An adhesive ECG electrode will be place on the study participant's right upper abdominal quadrant and then the patient cable reference electrode snap will be attached to the ECG electrode.
- The patient cable will then be connected to the EIT monitoring device (PulmoVista 500, Lubeck, Germany) via a color coded trunk cable orientation that aligns with the patient cable left and right orientation (See image).




- EIT device calibration and signal check
  - Researcher will initiate a PulmonVista 500 EIT monitoring device calibration each day prior to performing new study participant EELI measurements.
  - A skin-electrode signal check will be performed to ensure that a minimum of 15 of 16 electrodes have sufficient contact with the participant's skin surface and signal quality is stable. Researchers will use the following status display and explanation to determine adequacy of electrode contact and signal quality.




| Status | Explanation |
|---|---|
| Gray | Skin-electrode contact is sufficient for measurement to proceed |
| White | Skin-electrode contact is unstable, measurement will proceed but signal quality may be impaired |
| Red | Skin-electrode contact is insufficient for measurement to proceed |

- **Monitoring sessions and Lung Expansion Therapy procedure**

- Monitoring will be initiated after researcher performs PulmoVista 500 EIT device (Draeger; Lubeck, Germany) setup and calibration.
- Approximate monitoring/measurement duration is 15-minutes.

- **Lung expansion therapies will occur as follows:**
  - Study participants will sit with their back against a reclining chair with backrest adjust to 45-degrees.

- Two study investigators will be present during Incentive Spirometry and monitoring session. One study investigator will assist with EIT interface application and provide instruct study participants on how to perform I.S. therapy properly. A second study investigator will perform EIT device set-up and monitoring only.

**INCENTIVE SPIROMETRY GROUP**

- A study investigator will instruct the study participant to strive for an inspiratory capacity volume target as determined by the I.S. device's predicted volume nomogram table (See below).


**MALE**

HEIGHT IN INCHES

| AGE IN YEARS | 58" | 60" | 62" | 64" | 66" | 68" | 70" | 72" | 74" | 76" | 78" |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 20 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 | 3200 | 3400 | 3600 | 3800 | 4000 |
| 25 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 | 3350 | 3550 | 3750 | 3950 |
| 30 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 | 3500 | 3700 | 3900 |
| 35 | 1800 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 | 3200 | 3400 | 3600 | 3800 |
| 40 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 | 3350 | 3550 | 3750 |
| 45 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 | 3500 | 3700 |
| 50 | 1650 | 1850 | 2050 | 2250 | 2450 | 2650 | 2850 | 3050 | 3250 | 3450 | 3650 |
| 55 | 1550 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 | 3350 | 3550 |
| 60 | 1500 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 | 3500 |
| 65 | 1400 | 1600 | 1800 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 | 3200 | 3400 |
| 70 | 1350 | 1550 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 | 3350 |
| 75 | 1300 | 1500 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 |
| 80 | 1250 | 1450 | 1650 | 1850 | 2050 | 2250 | 2450 | 2650 | 2850 | 2050 | 3250 |

**FEMALE**

HEIGHT IN INCHES

| AGE IN YEARS | 58" | 60" | 62" | 64" | 66" | 68" | 70" | 72" | 74" |
|---|---|---|---|---|---|---|---|---|---|
| 20 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 | 3500 |
| 25 | 1850 | 2050 | 2250 | 2450 | 2650 | 2850 | 3050 | 3250 | 3450 |
| 30 | 1800 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 | 3200 | 3400 |
| 35 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 | 3350 |
| 40 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 | 3300 |
| 45 | 1650 | 1850 | 2050 | 2250 | 2450 | 2650 | 2850 | 3050 | 3250 |
| 50 | 1600 | 1800 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 | 3200 |
| 55 | 1550 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 | 3150 |
| 60 | 1500 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 | 3100 |
| 65 | 1450 | 1650 | 1850 | 2050 | 2250 | 2450 | 2650 | 2850 | 3050 |
| 70 | 1400 | 1600 | 1800 | 2000 | 2200 | 2400 | 2600 | 2800 | 3000 |
| 75 | 1350 | 1550 | 1750 | 1950 | 2150 | 2350 | 2550 | 2750 | 2950 |
| 80 | 1300 | 1500 | 1700 | 1900 | 2100 | 2300 | 2500 | 2700 | 2900 |

**Incentive Spirometry procedure**

A study investigator will provide instruction on Incentive Spirometry procedure performance before supervised therapy and monitoring begins.

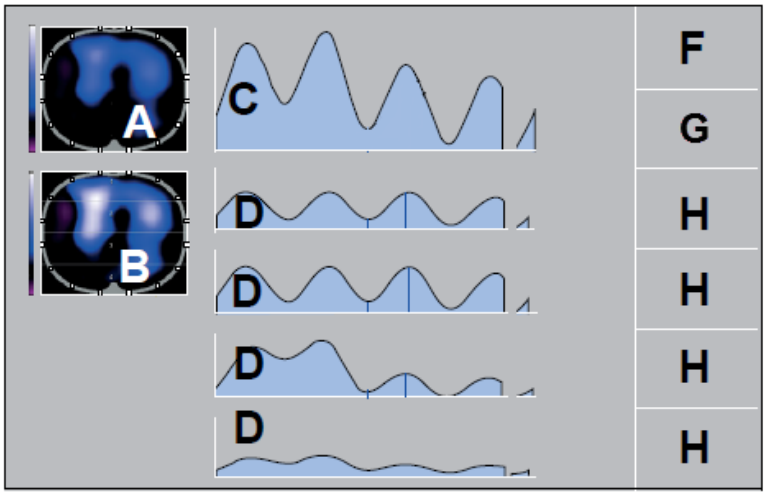
- Five minutes of eupneic ventilation EIT monitoring will occur before I.S. therapy commences.
- Study participants will be asked to take 10 deep breaths through the incentive spirometer's mouthpiece, followed by a 60 second pause.
- The 10-breath cycle will be repeated three times with respiratory therapist coaching.
- Five minutes of eupneic ventilation EIT monitoring will occur following the last I.S. lung expansion therapy breath cycle.
- Incentive Spirometry therapy and monitoring session will last about 15 minutes (See image).

**EzPAP® POSITIVE AIRWAY PRESSURE GROUP**

- A study investigator will provide instruction on EzPAP® procedure performance before supervised therapy and monitoring begins. A second study investigator will perform EIT device set-up and monitoring only.
- Five minutes of eupneic ventilation EIT monitoring will occur before EzPAP® therapy commences.
- Study participants will be asked to breathe normally through the EzPAP® device's mouthpiece for 10 breaths, followed by a 60 second pause.
- The 10-breath cycle will be repeated three times with respiratory therapist coaching.
- Five minutes of eupneic ventilation EIT monitoring will occur following the last EzPAP® lung expansion therapy breath cycle.
- EzPAP® therapy and monitoring sessions will last about 15 minutes (See image).

**REGIONAL DISTRIBUTION OF VENTILATION MONITORING:**

- PulmoVista monitoring and lung expansion therapy will occur only one time as described above. .
- The following information will be displayed on the PulmoVista 500 device's main monitoring screen during lung expansion therapy, but study investigator staff administering therapy and study participants will be blinded from information displayed on the screen's monitor during therapy session in an effort to reduce performance bias:

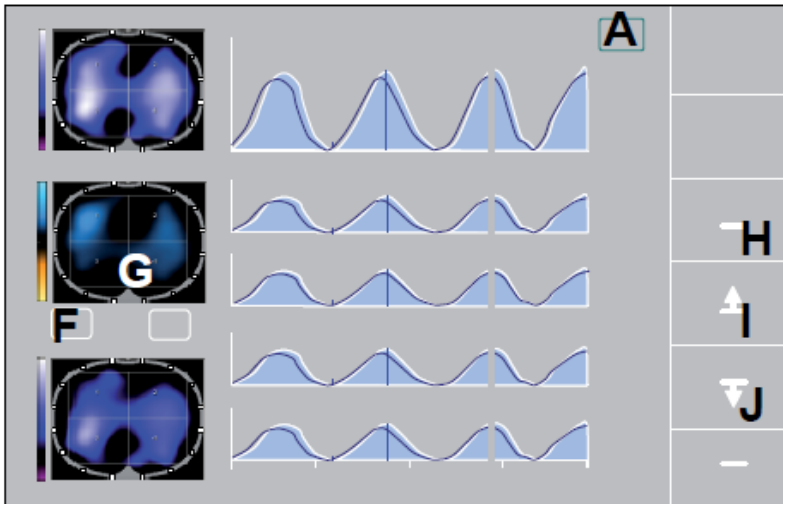



A: Dynamic imaging showing impedance changes in a caudo-cranial image referenced to a dynamic basline.
B: Tidal image showing EELI during inspiration and exhalation of the last detected breath.
C: Global impedance waveform showing relative impedance changes across electrode plane.
D: Regional impedance waveforms
F: Tidal respiratory rate
G: Global tidal variation displayed as 100%.
H: Regional tidal variation displayed as a percentage of global tidal variation.

- Once lung expansion therapy

session has ended, the researcher will detach trunk cables from electrode cables, detach reference electrode snap from adhesive ECG electrode, unclamp the electrode belt, and then remove belt from the study subject. Subject participation in this study is considered complete at this time.
- Inspect of electrode belt contact area will be performed to assess for evidence of skin irritation or bruising. Study participant will be notified by study investigator at the time of skin assessment if significant skin irritation or bruising is present. Finding will be recorded by study investigator.

- Displaying changes
  - The following information will be displayed and used to record pre and post lung expansion therapy end-expiratory lung impedance changes:




A: Reference button
F: Display change
G: Differences between status image and reference image. EELI changes displayed with regional color changes on image.

Deviation from regional ventilation reference parameter region (Ex: dorsal EELI) :
H: No change in EELI %
I: Increased EELI %
J: Decreased EELI %

- Electrode belt, patient cable, and PulmoVista 500 EIT device (Draeger; Lubeck, Germany) will be removed study participant's room and returned to a storage location outside of patient care areas.
- Following each EIT to subject interface disconnect, an alcohol, aldehyde, or quaternary ammonium based compound will be soaked on a wipe cloth to disinfect the surfaces of the patient cable, electrode belt, trunk cable, and EIT unit.

**2. List the procedures, in bullet form, that will be done for <u>RESEARCH PURPOSES</u> as stipulated in this protocol.**

**INSTRUCTIONS:**
Examples: blood tests, EKG, x-rays, surveys, administration of investigational drug/device, randomization to one of two approved drugs
**Do NOT list those procedures which are being ordered for clinical standard of care.**
If ALL procedures are being done for the research study, simply write: ALL

Answer/Response: All

**3. Do you confirm that, except for blood draws through a peripheral site, that all invasive procedures will be performed by a licensed health care provider under the supervision of an MD?**
Answer/Response: N/A, no invasive procedures done for this study.

**4. Will you be using data/specimens in this study that were collected previously, with the use of a research consent form, from another research study?**
Answer/Response: No

**IF YES, will the data/specimens be used in this study without a new consent from the original donor?**
Answer/Response:

**IF YES, explain how the proposed use is consistent with the use planned in this study and submit a copy of the consent form used to collect the data/specimens.**

**INSTRUCTIONS:** If you are unable to locate the consent form, you must request a Waiver of Consent. Consult with IRB staff to determine additional sections to be added to this protocol.

Answer/Response:

**5. Will any of the procedures listed in item # 2 have the potential to identify an incidental finding? This includes ALL procedures, assessments and evaluations that are being done for <u>RESEARCH PURPOSES</u> that may or may not be considered investigational.**

**Examples:** MRI/CT/PET/CXR shows possible tumor, Blood collected and analyzed using an investigational assay, Blood tests show possibility of leukemia, Surveys which reveal depression/ suicidal tendencies.

Answer/Response: No

►IF YES, *check one of the following two options:*

_____The examination(s) utilize(s) the same techniques, equipment, etc., that would be used if the subject were to have the examination(s) performed for clinical care. **There exists the potential for the discovery of clinically significant incidental findings.**

- The PI takes full responsibility for the identification of incidental findings:
- The PI will inform the subjects verbally of all incidental findings that are of clinical significance or are of questionable significance**.**
- A follow-up letter describing the finding should be provided to the subject with instructions to either show the letter to their PC or if the subject has no PCP, the subject should be instructed to make an appointment at UVa or at the Free Clinic**.**

____This examination(s) utilizes non-standard/investigational, technique, equipment, etc. It is impossible to determine the significance of such results, therefore abnormalities will not be shared with study participants because the meaning of the exam is not yet proven and is of unknown clinical benefit.

**6. Do any of the procedures listed above, under question # 2, utilize any imaging procedures for <u>RESEARCH PURPOSES</u>?**

**Examples:** ultrasound, CT scans/ x-rays etc.

Answer/Response: Yes.

**IF YES, list procedures:**

Answer/Response:

Non-radiating Electrical Impedance Tomography (EIT)

►IF YES, *check one of the following two options:*

_____This imaging research examination utilizes the same imaging techniques, equipment, scanning sequences that would be used if the subject were to have the imaging performed for clinical care. There exists the potential for the discovery of clinically significant incidental findings.

►If checked, answer the following:

**Will the images be read by a licensed radiologist and the reading placed in the subject's medical record?**

Answer/Response:

►IF NO: The PI takes full responsibility for the identification of incidental findings:

- The PI will have all incidental findings reviewed by a radiologist who will advise the PI regarding clinical significance.
- The PI will inform the subjects verbally of all incidental findings that are of clinical significance or are of questionable significance**.**
- A follow-up letter describing the finding should be provided t**o t**he subject with instructions to either show the letter to their PC or if the subject has **no** PCP, the subject should be instructed to make an appointment at UVa or at the Free Clinic.

__**X**___This imaging research examination utilizes non-standard/investigational imaging modality, techniques, equipment, scanning sequences, etc. It is impossible to determine the significance of such images, therefore abnormalities will not be shared with the subject because the meaning of the exam is not yet proven and is of unknown clinical benefit.

**7. Will you be using viable embryos?**

IF YES, attach approval from UVA ESCRO Committee

Answer/Response: No

**8. Will you be using embryonic stem cells?**

IF YES, attach approval from UVA ESCRO Committee

Answer/Response: No

**9 Are any aspects of the study kept secret from the participants?**

Answer/Response: No

►**IF YES, describe:**

Answer/Response:

**10. Is any deception used in the study?**

Answer/Response: No

►**IF YES, describe:**

**INSTRUCTIONS:** Describe the deception involved and the debrief procedures. Attach a post-experiment debriefing statement and consent form offering participants the option of having data destroyed.

Answer/Response:

**11. If this protocol involves study treatment, explain how a subject will be transitioned from study treatment when they have completed their participation in the study.**

**Example:** If the subject will be taking an investigational drug, will they need to be put back on an approved drug when they have completed the study? If yes, explain how this will be accomplished and who will cover the cost. If the subject has a device implanted will it be removed? Again- who will cover the cost of the removal?
**Instructions:** Answer NA if this study does not involve a study treatment.

Answer/Response: N/A

**12. Will your study involve measures (C-SSRS/BID/SCID etc.) used to assess for depression and/or suicidality <u>for research purposes?</u>** No

**Answer this question YES if any of the following apply:**

1) The protocol has a research purpose to study suicide, suicidal ideation, depression or trauma
2) The protocol has a research purpose to study traumatic life events that may evoke powerful emotion or induce mood changes in participants;
3) The protocol includes **assessments** (e.g. Surveys, exams, questionnaires, etc.) that can be used to identify **depression and/or suicidal ideation** (thoughts of suicide, either active or passive), plan (the means or mechanism) or intent (the expressed desire and willingness to act on the plan).

**IF YES:**

a. Which research staff members are qualified to assess suicidality/depression and will be available to provide care and intervention?

Answer/Response:

b. Include specific guidelines for intervention based on assessment tools and rating scales. (i.e. based on C-SSRS/BID, SCID score of xxx, subject will be assessed further by the PI for suicide risk or referred urgently to an ED, crisis center, or clinic immediately).
Answer/Response:

c. Describe a plan to link participants to psychological help if needed and include written materials listing those resources as an attachment to the protocol. This plan should include details of the planned interventions for differing severities of depression or suicidality, including a plan for how imminent risk of harm will be handled for the study's targeted population. (May include a list of local psychiatry/psychotherapy providers at UVA). **Note: If the subject is a patient at UVA Medical Center, you must adhere to Medical Center Policy 0140 Judicial Treatment Order and 0197 Suicide Risk Assessment and Prevention**.
Answer/Response:

d. Describe a plan to address the situation if a participant is assessed to be a danger to themselves, but refuses treatment. (the plan may include steps to contact 911)
**Note: If the subject is a patient at UVA Medical Center, you must adhere to you must adhere to Medical Center Policy 0140 Judicial Treatment Order and 0197 Suicide Risk Assessment and Prevention.**
Answer/Response:

e. Will subjects, who discontinue or are withdrawn secondary to suicidal ideations/depression prior to study completion, be asked to come to the site for an early withdrawal visit as soon as possible?
Answer/Response:

**If No**, provide outline of plan for follow-up or indicate if follow up is not required.

13. **Where will the study procedures be done?**
Check One:
____ UVA medical center facilities ( In patient or outpatient)
____ UVa , but not medical center facilities: LIST specific location Answer/Response:
___X_ Other LIST specific location Answer/Response: University of Virginia Medical Center, Second Floor, Pulmonary Diagnostics & Respiratory Therapy Services, Room 2025.

**14. If the study involves medical risk and study procedures will be done outside of the UVa Medical Center what is your plan to protect the subjects in case of a medical emergency?**
*Check all applicable options:*
_____ MD, RN, onsite during procedures
_____ Individual trained in CPR on site during procedures
_____ AED and Individual trained to use it onsite
_____ Call 911
_X____ Other : Describe Answer/Response: N/A, no medical risks

## Data and Safety Monitoring Plan

This study has been deemed minimal risk. Because this study poses minimal risk to the subject, **adverse events will only be collected or recorded if a causal relationship to the study intervention is suspected.** If any adverse event is considered serious and unexpected, the event must be reported to the IRB-HSR within 7 days from the time the study team receives knowledge of the event.

### 1. Definitions

#### 1.1 How will you define adverse events (AE)?

Do not change this answer

An adverse event will be considered any undesirable sign, symptom or medical condition considered **related to the intervention**. Medical condition/diseases present before starting the intervention will be considered adverse events only if they worsen after starting the study and that worsening is considered to be related to the study intervention. An adverse event is also any undesirable and unintended effect of research occurring in human subjects as a result of the collection of identifiable private information under the research.

#### 1.2 How will you define an unanticipated problem?

Do not change this answer

An unanticipated problem is any issue that involves increased risk(s) to participants or others. This means issues or problems that cause the subject or others to be placed at greater risk than previously identified, even if the subject or others do not incur actual harm. For example if a subject's confidentiality is compromised resulting in serious negative social, legal or economic ramifications, an unanticipated problem would need to be reported. (e.g serious loss of social status, loss of job, interpersonal conflict.)

#### 1.3 What are the definitions of a protocol violation and/or noncompliance?

Do not change this answer

**A protocol violation** is defined as any change, deviation, or departure from the study design or procedures of research project that is NOT approved by the IRB-HSR prior to its initiation or implementation**.** Protocol violations may be major or minor violations.

**Noncompliance** can be a protocol violation OR deviation from standard operating procedures, Good Clinical Practices (GCPs), federal, state or local regulation**s.** Noncompliance may be serious or continuing

Additional Information: see the IRB-HSR website at http://www.virginia.edu/vpr/irb/HSR_docs/Forms/Protocol_Violations_%20Enrollment_Exceptions_Instructions.doc

#### 1.4 What is the definition of a data breach?

| Do not change this answer |
|---|
| A data breach is defined in the HITECH Act (43 USC 17932) as an unauthorized acquisition, access, or use of protected health information (PHI) that compromises the security or privacy of such information. |
| Additional Information may be found on the IRB-HSR Website: Data Breach |

**2. What risks are expected due to the intervention in this protocol?**

INSTRUCTIONS:

- The risks should be consistent with those in the consent form (if applicable), although they should be written in technical terms in the protocol and in lay terminology in the consent form.
- List the most serious or most frequent risk first
- Delete last two rows if no additional risks added.
- Add additional rows to the table below if needed.

| **Expected Risks related to study participation** | **Pick One** |
|---|---|
| There is a small risk that breaches of privacy and/or confidentiality might occur. The risk of violation of subject privacy and confidentiality is minimal due to the requirements of the privacy plan in this protocol. | Occurs rarely |
| • Skin irritation that continues for greater than 1-hour after electrode belt is removed.<br>• Decreased lung volume resulting from patient belt surrounding thoracic cavity. | Occurs frequently,<br>Occurs infrequently<br>X Occurs rarely |
| Violation of subject's privacy and confidentiality:<br>- Study participant related data will be de-identified and assigned a unique study identifier (I.D.) in ascending order of enrollment. I.D. range: 1 – 120.<br><br>The unique ID will be entered into the PulmoVista 500. Recorded raw data will be transferred to an | Minimized due to the requirements of this protocol. |

| | |
|---|---|
| encrypted and password protected electronic media drive (USB drive). The password will be known only by our U. VA Medical Center EIT research team members. The collected data may be communicated for the purposes of the study, according to informed consent and clinical trials agreement with Draeger Medical. | |

**3. When will recording and reporting of unanticipated problems/adverse events begin?**

_____After subject signs consent

__X___ After subject begins study intervention

_____Other Specify Answer/Response:

**4. When will the recording/reporting of unanticipated problems/adverse events end?**

__X___Subject completes participation in the protocol

_____End of intervention

_____30 days post intervention

_____Subject completes intervention and follow up period of protocol

_____Other: Specify Answer/Response:

**5. What is your plan for safety monitoring?**

Do not change this answer

Safety monitoring and aggregate review of adverse events, unanticipated problems, protocol violations and any data breach will be performed by the PI and IRB-HSR through continuation review at least annually.

**6. What is your plan for reporting a Unanticipated Problem, Protocol Violation or Data Breach?**

Do not change this answer

| Type of Event | To whom will it be reported: | Time Frame for Reporting | How reported? |
|---|---|---|---|
| **Unanticipated Problems** tha are not adverse events or protocol violations This would include a Data | IRB-HSR | Within 7 calendar days from the time the study team received knowledge | Unanticipated Problem report form. *http://www.virginia.edu/vprgs/i* |

| | | | |
|---|---|---|---|
| Breach. | | of the event. | *rb/HSR_docs/Forms/Reporting_Requirements-Unanticipated_Problems.doc )* |
| **Protocol Violations/Noncompliance** (*The IRB-HSR only requires that MAJOR violation be reported, unless otherwise required by your sponsor, if applicable.)* | IRB-HSR | Within 7 calendar days from the time the study team received knowledge of the event. | Protocol Violation, Noncompliance and Enrollment Exception Reporting Form<br><br>*http://www.virginia.edu/vprgs/irb/hsr_forms.html*<br><br>*Go to 3rd bullet from the bottom.* |
| **Data Breach** of Protected Health Information | The UVa Corporate Compliance and Privacy Office<br><br>ITC: if breach involves electronic data<br><br>Police if breach includes items that are stolen:<br><br>Stolen on UVA Grounds<br><br>OR<br><br>Stolen off UVa Grounds- contact police department of jurisdiction of last known location of PHI | As soon as possible and no later than 24 hours from the time the incident is identified.<br><br>As soon as possible and no later than 24 hours from the time the incident is identified.<br><br>IMMEDIATELY. | UVa Corporate Compliance and Privacy Office- Phone 924-9741<br><br>**ITC:** Information Security Incident Reporting procedure, http://www.itc.virginia.edu/security/reporting.html<br><br>Police: phone- (434) 924-7166 |

## Risk/ Benefit Analysis

**1. What are the potential benefits for the participant as well as benefits which may accrue to society in general, as a result of this study?**

Answer/Response:

While participants will not benefit directly from this study, we anticipate that important information will be gained from our EIT monitoring of regional distribution of ventilation. Future patients may benefit from our study findings as we hope to advance clinical understandings associated with these

therapies with use of EIT monitoring. Our findings also have potential to reduce the use of clinically ineffective lung expansion therapy, which has potential for more appropriate utilization of health care resources, benefitting society in general.

The potential benefit for study participants will not be realized directly since our aim is to monitor regional distribution of ventilation in response to I.S. or EzPAP® lung expansion therapy. These therapies are considered to be standards of care in post-operative surgical patients. Loss of dorsal regional lung volume (i.e., atelectasis) is an example of a post-operative pulmonary complication. EzPAP® is a lung expansion therapy that is used as an alternative to I.S. lung expansion therapy for increasing dorsal regional lung volume (i.e., functional residual capacity) in an effort to prevent or reverse atelectasis. When expiratory positive airway pressures of 5, 10, and 15 cmH2O was administered to a small group of healthy human subjects, Garrard et al. (Chest, 1978) found a positive pressure of 15 cmH2O was associated with the greatest FRC increase when compared to zero pressure and baseline FRC measurements. We are unable to identify previous research describing whether regional redistribution of ventilation is sustained after completing I.S. or EzPAP lung expansion therapy.

**2. Do the anticipated benefits justify asking subjects to undertake the risks?**

**INSTRUCTIONS:** Analyze the risk-benefit ratio and justify your answer.
Analyze the risk- benefit of interventions offering potential health benefit separately from those done solely to answer a research question or generate generalizable knowledge. Clarify risk-benefit for direct benefit to individual participant versus benefit to society.

Answer/Response: Yes. There are minimal risks and a potential for societal benefit.

## Bibliography

**INSTRUCTIONS:** Provide a current bibliography supporting the hypothesis, background and methodology including references to papers and abstracts that have resulted from previous work by the investigator and references to the work of others.

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Stankiewicz-Rudnicki, M., Gaszynski, T., & Gaszynski, W. (2015). Assessment of regional ventilation in acute respiratory distress syndrome by electrical impedance tomography. Anaesthesiology Intensive Therapy, 47(1), 77-81. doi:10.5603/AIT.2015.0007 [doi]

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Westerdahl, E., Lindmark, B., Eriksson, T., Friberg, O., Hedenstierna, G., & Tenling, A. (2005). Deep-breathing exercises reduce atelectasis and improve pulmonary function after coronary artery bypass surgery. *Chest, 128*(5), 3482-3488. doi:128/5/3482 [pii]

## APPENDIX: Support Source

INSTRUCTIONS: The support source is any source outside of UVA providing support such as supplies/drug/device's or financial assistance. The entity should NOT be considered a Support Source if they are taking on the responsibilities of a sponsor such as monitoring, safety oversight or data analysis. Do not enter a company/ organization as a supply source unless the support has been secured. The IRB-HSR must be notified and the consent form revised if a support source changes. (Example-the NIH or an investigator-initiated study in which the pharmaceutical company is providing drug free of charge.)

1. **Describe what will be provided and by whom**.
   Answer/Response: PulmoVista 500 Electrical Impedance Tomography device (Draeger; Lubeck, Germany)

2. **Do you confirm that you will obtain a contract/ material transfer agreement with the provider via the Medical Center Procurement office or Office of Sponsored Programs (OSP) ospnoa@virginia.edu?**

| |
|---|
| INSTRUCTIONS:<br>You should have answered YES to the following question in Protocol Builder:<br>*--"Do you/will you have a contract with an outside entity to support this protocol?"*<br><br>Work with Medical Center Procurement on the agreement if the item will be used on a patient in the Medical Center.<br>Work with OSP on the contract is the item will be used outside of the Medical Center. |

Answer/Response: Yes

## APPENDIX: Legal/Regulatory

**Recruitment**

The following procedures will be followed:

- Finders fees will not be paid to an individual as they are not allowed by UVa Policy.
- All recruitment materials will be approved by the IRB-HSR prior to use. They will be submitted to the IRB after the IRB-HSR has assigned an IRB-HSR # to the protocol.
- Only those individuals listed as personnel on this protocol will recruit and or conduct the consenting process with potential subjects.

**Retention Incentives**

Any item used by the sponsor/ study team to provide incentive to a subject to remain in the study, other than compensation identified in the Payment section, will be submitted to the IRB for review prior to use. The IRB-HSR will provide the study team with a Receipt Acknowledgement for their records. Retention incentive items are such things as water bottles, small tote bags, birthday cards etc. Cash and gift cards are not allowed as retention incentives.

**Clinical Privileges**

The following procedures will be followed:

- Investigators who are members of the clinical staff at the University of Virginia Medical Center must have the appropriate credentials and been granted clinical privileges to perform specific clinical procedures whether those procedures are experimental or standard.
- The IRB cannot grant clinical privileges.
- Performing procedures which are outside the scope of the clinical privileges that have been granted may result in denial of insurance coverage should claims of negligence or malpractice arise.
- Personnel on this protocol will have the appropriate credentials and clinical privileges in place before performing any procedures required by this protocol.
- Contact the Clinical Staff Office- 924-9055 or 924-8778 for further information.

**Sharing of Data/Specimens**

Data and specimens collected under an IRB approved protocol are the property of the University of Virginia. You must have "permission" to share data/ specimens outside of UVa other than for a

grant application and or publication. This "permission" may come in the form of a contract with the sponsor or a material transfer agreement (MTA) with others. A contract/ MTA is needed to share the data outside of UVa even if the data includes no HIPAA identifiers and no code that could link the data back to a HIPAA identifier.

- No data will be shared outside of UVa, beyond using data for a grant application and or publication, without a signed contract/MTA approved by the SOM Grants and Contracts office/ OSP or written confirmation that one is not needed.
- No specimens will be shared outside of UVa without a signed contract/MTA approved by the SOM Grants and Contracts office/ OSP or written confirmation that one is not needed.

**Prisoners**

If the original protocol/ IRB application stated that no prisoners would be enrolled in this study and subsequently a subject becomes a prisoner, the study team must notify the IRB immediately. The study team and IRB will need to determine if the subject will remain in the study. If the subject will remain in the study, the protocol will have to be re-reviewed with the input of a prisoner advocate. The prisoner advocate will also have to be involved in the review of future continuations, modifications or any other reporting such as protocol violations or adverse events.

Prisoner- Individuals are prisoners if they are in any kind of penal institution, such as a prison, jail, or juvenile offender facility, and their ability to leave the institution is restricted. Prisoners may be convicted felons, or may be untried persons who are detained pending judicial action, for example, arraignment or trial.
For additional information see the OHRP website at
http://www.hhs.gov/ohrp/policy/populations/index.html

**Compensation in Case of Injury**

If a subject requests compensation for an injury, the study team should notify the IRB-HSR (924-9634/2439847) the UVa Health System Patient Relations Department (924-8315). As a proactive courtesy, the study team may also notify UVa Health System Patient Safety and Risk Management (924-5595).

On request, the study team should provide the Risk Management Office with the following information/documents:

- Subject Name and Medical Record Number
- Research medical records
- Research consent form
- Adverse event report to IRB
- Any letter from IRB to OHRP

**Subject Complaints**

During a research study, the study team may receive complaints from a subject. If the study team is uncertain how to respond to a complaint, or is unable to resolve it with the subject, the study team may contact the IRB-HSR (924-9634/243-9847), the UVa Health System Patient Relations Department (924-8315).

**Request for Research Records from Search Warrant or Subpoena**

If the study team receives a request for research records from a search warrant or subpoena, they should notify UVa Health Information Services at 924-5136. It is important to notify them if information from the study is protected by a Certificate of Confidentiality.

## APPENDIX: Unapproved Device Use

## (Unapproved Device being used but not evaluated)

**INSTRUCTIONS:** This section is to provide the IRB with information about the safety of a device that is being USED, but not evaluated in this study for safety and efficacy. The device may have FDA approval and is being used for a non-approved indication OR the device may not have FDA approval [these are typically known as Research Use Only (RUO) Devices]. Again the RUO Device is only being USED and NOT being evaluated for safety and efficacy in this study. The information below will be used by the IRB to make a minimal risk determination regarding this protocol.

1. **List name of device(s) being used in an unapproved manner in this protocol**.

Per the statute: Federal Food, Drug, and Cosmetic Act Sec 201.h [21USC321]
DEVICE: (h) The term "device" (except when used in paragraph (n) of this section and in sections 301(i), 403(f), 502(c), and 602(c)) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—
(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
(2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
(3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Answer/Response: PulmoVista 500 Electrical Impedance Tomography device (Draeger; Lubeck, Germany). This device is not approved by the FDA, however, the device is approved for clinical use in Canada, China, and European countries. It is not commercially available for use in the U.S. Health System.

2. **Do you confirm the device is only being USED and NOT being evaluated in this study?**
Answer/Response: Yes

3. **Is the device a Research Use Only (RUO) device?**

IF YES, submit the manufactures brochure/information regarding the RUO with other documents at the time of pre-review.
IMPORTANT: The RUO designation is made by the FDA.
The package insert MUST stipulate that this is a RUO device.

Answer/Response: No

►**If the device is a RUO device, do you agree to use the device according to instructions in the manufacturers brochure?**
Answer/Response: N/A

►**If the device is NOT a RUO device, is the device currently approved for any indication?**
Answer/Response: Yes. This device is approved for the indication used in the study in other countries but is not approved by the FDA.

►**If the device is currently approved list the indication:**

| **INSTRUCTIONS:** Also submit the Manufacturer's Brochure |
|---|

Answer/Response: Drägers PulmoVista 500 provides EIT lung monitoring and is used in many hospitals all over the globe.

►**If the device is currently approved, do you confirm that results will not be used in clinical care of the subject (e.g. will not be used for diagnosis or treatment?)**
Answer/Response: Yes.

4. **In how many humans has this device been used previously as it is being used in this study?**
Answer/Response: Unknown. However, the device is approved for clinical use in Canada, China, and European countries. There are four PulmoVista EIT device clinical trials registered from within the United States on ClinicalTrials.gov; Two at Boston Children's Hospital, one at Unity Point in Delaware, a current study being performed by our research group here at the University of Virginia Medical Center.

5. **Describe pertinent human data that is available regarding the safety of this device as you are using it in this protocol.**
Answer/Response: Validation studies and published clinical trials using PulmoVista 500 EIT device (Draeger; Lubeck, Germany) for measuring lung volume distribution in mechanically ventilated and non-mechanically ventilated human subjects signifies low patient risk. Examples include Victoriano (2004) and Riedel (2005) validation studies that aimed to evaluate EIT detection of lung volume distribution in comparison with CT images. Related to our study, EIT monitoring has good correlation with regional lung volume changes.

6. **If this protocol will be used in children, describe any previous use of this device with children of a similar age range as it is being used in this study.**
Answer/Response: NA

7. **What steps will be taken to minimize risk?**
Answer/Response: Each study investigator has/will receive PulmoVista 500 EIT device (Draeger; Lubeck, Germany) didactic and clinical simulation training on how to prepare study participants for monitoring (i.e., determining electrode belt and cable selection), how to properly calibrate and operate the device, and how interpret, record, and download data to a password encrypted storage drive. Respiratory Therapy study investigators are content

experts with I.S. and EzPAP® training as these are lung expansion therapy standards of practice used at the University of Virginia Medical Center.

**8. Would you consider the use of this device to be minimal risk? Why or why not?**

Minimal Risk: probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. 45CFR46.102

Answer/Response: Yes. The PulmoVista 500 EIT device (Draeger; Lubeck, Germany) is a monitoring tool with animal and human subject validation studies reporting good measurement correlation when compared with CT images. It is non-invasive and non-radiation producing.

## APPENDIX: Recruitment

Recruitment includes identifying, review of records to determine eligibility or any contact to determine a potential subjects interest in the study.

*The UVa HIPAA covered entity is composed of the UVa VP Office of Research, the Health System, School of Medicine, School of Nursing, Nutrition Services (Morrisons), the Sheila C. Johnson Center, the Exercise and Sports Injury Laboratory and the Exercise Physiology Laboratory.

**1. How do you plan to <u>identify</u> potential subjects?**

- To "identify" a potential subject refers to steps you plan to take to determine which individuals would qualify to participate in your study. This does NOT include steps to actually contact those individuals.
- If your study involves more than one group of subjects (e.g. controls and cases or subjects and caregivers) note below which groups are being identified by the given method.
- Check the methods you plan to utilize:

a.____ Chart Review/ Clinic Schedule Review/ Database Review from a database established for health care operations (departmental clinical database) or an Improvement Project (*e.g. Performance Improvement, Practice Improvement, Quality Improvement*).
*<u>If you plan to obtain data from the UVa Enterprise Data Warehouse (EDW) please see option b below.</u>*

<u>DHHS:</u> Study team requests Waiver of Consent to identify potential subjects.

<u>HIPAA:</u> Allowed under Preparatory to Research if PHI to be accessed.

<u>IMPORTANT</u>

Keep in mind that PHI in the medical record may only be accessed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

b____ Review of a database that was established to keep data to be used for future research such as the CDR, departmental research database or use of data from a separate current active research protocol.
*If you plan to obtain data from the UVa Enterprise Data Warehouse (EDW) you are required to submit your request to the CDR. The CDR staff will work with the EDW to obtain the data you need.*

DHHS: Study team requests Waiver of Consent to identify potential subjects.

HIPAA: Allowed under Preparatory to Research if PHI to be accessed.

IMPORTANT
Keep in mind that PHI in the medical record may only be accessed by individuals who work under the UVa HIPAA covered entity; which means they who meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

The information from which you are obtaining potential subjects must also have an IRB protocol approval. If this item is checked, enter the IRB # below.

**IRB#** _____

If obtaining information from the Clinical Data Repository (CDR) insert IRB # 10797

c. ____ Patients UVa health care provider supplies the UVa study team with the patients contact information without patients' knowledge.

DHHS: Study team requests Waiver of Consent to identify potential subjects.

HIPAA: Allowed under Preparatory to Research if PHI will be shared by the health care provider.

IMPORTANT
Keep in mind that PHI may only be given to individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:

--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

d. ____ Patient obtains information about the study from their health care provider. The patient contacts the study team if interested in participating. (Health care provider may or may not also be the a member of the study team)

DHHS: NA
HIPAA: Allowed under Health Care Operations

If this choice is checked, check 3d-INDIRECT CONTACT below.

e. __X__ Potential subjects will not be directly identified. They will respond to an advertisement such as a flyer, brochure etc.

If this choice is checked, check 3d- INDIRECT CONTACT below.
DHHS & HIPAA: NA

f. _____ Potential subjects have previously signed a consent to have their name in a registry/database to be contacted for future studies of this type.

**IRB# of registry/ database:** _____

DHHS & HIPAA: NA

g. __X__ Other: Specify Answer/Response: Potential subjects are not patients.

**If item # a, b or c is checked above and if this protocol involves the use of protected health information do you confirm the following to be true?**

- The use or disclosure is sought solely to review protected health information as necessary to prepare the research protocol or other similar preparatory purposes.
- No PHI will be removed from the UVa covered entity.
- The PHI that the researcher seeks to use or access is necessary for the research purposes.

Answer/Response:

**2. How will potential subjects be contacted?**

To "contact" a potential subjects refers to the initial contact you plan to take to reach a potential subject to determine if they would be interested in participating in your study. This may include direct contact by such methods as by letter, phone, email or in-person or indirect contact such as the use of flyers, radio ads etc.

If your study involves more than one group of subjects (e.g. controls and cases or subjects and caregivers) note below which groups are being contacted by the given method.

Check the methods below you plan to utilize:

a.____Direct contact of potential subjects by the study team via letter, phone, direct e-mail. Members of study team ARE NOT health care providers of patients. Information will not be collected from psychotherapy notes.

Note: Letter, phone, direct email scripts must be approved by IRB prior to use. See IRB-HSR Website for templates.

DHHS/HIPAA: Study team requests a Waiver of Consent and Waiver of HIPAA Authorization to contact potential subjects.

IMPORTANT:
Keep in mind that if PHI was collected during the identification phase that contact with potential subjects may only be performed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:

- a UVa student working in the UVa HIPAA Covered Entity*
- a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

b.____Potential subjects will be approached while at UVa Hospital or Health Clinic by a person who is NOT a member of their health care team. Information will not be collected from psychotherapy notes.

DHHS & HIPAA: Study team requests a Waiver of Consent and a Waiver of HIPAA Authorization to contact potential subjects.

IMPORTANT:
Keep in mind that contacting individuals in a clinical setting may only be performed by individuals who work under the UVa HIPAA covered entity; which means they meet one of the following criteria:
a UVa student working in the UVa HIPAA Covered Entity*
a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

You should share the following information with the potential subject:

- Your name
- Who you are: physician, nurse etc. at the University of Virginia.
- Why you want to speak with them
- Ask if you have their permission to explain the study to them

- If asked about how you obtained their information use one of the following as an option for response.
  - DO NOT USE THIS RESPONSE UNLESS YOU HAVE OBTAINED PERMISSION FROM THEIR UVa PHYSICIAN: Your doctor, Dr. insert name wanted you to be aware of this research study and gave us permission to contact you.
  - We obtained your information from your medical records at UVa.
  - Federal regulations allow the UVa Health System to release your information to researchers at UVa, so that we may contact you regarding studies you may be interested in participating. We want to assure you that we will keep your information confidential.
- IF THE PERSON SEEMS ANGRY, HESITANT OR UPSET, THANK THEM FOR THEIR TIME AND DO NOT ENROLL THEM IN THE STUDY. YOU MAY ALSO REFER THEM TO THE IRB-HSR AT 924-9634.

c.____Direct contact of potential subjects by the study team by approaching in person at UVa or via letter, phone, direct e-mail. Members of study team contacting potential subjects ARE health care providers of patients.

If you are not approaching them in person but using a letter, phone call or direct email please note that the letter, phone, direct email scripts must be approved by IRB prior to use.
See IRB-HSR Website for templates.

DHHS: Study team requests a Waiver of Consent to contact potential subjects
HIPAA: Allowed under Health Care Operations.

d._X___ Indirect contact (flyer, brochure, TV, broadcast emails, patient provided info about the study from their health care provider and either the patient contacts study team or gives their healthcare provider permission for the study team to contact them.)

The indirect method used (flyer, brochure, TV, broadcast emails) must be approved by the IRB prior to use. The IRB does not need to review any type of script to use when the potential subject responds to the indirect method.

DHHS & HIPAA: NA

e. __X__ Potential subjects are not patients. The study does not include obtaining subjects health information. Subjects will be contacted directly

via email, phone, letter or presentation in group setting with consent then obtained individually in a private setting.

If you are not approaching them in person but using a letter, phone call or direct email please note that the letter, phone, direct email scripts must be approved by IRB prior to use.
See IRB-HSR Website for templates.

DHHS: Study team requests a Waiver of Consent to contact potential subjects.
HIPPA: NA

3. **Will any additional information be obtained from a potential subject during "prescreening"?**

**Pre-screening** for IRB purposes is the term used to describe activities PRIOR to obtaining Informed Consent and may not include any research procedures.

The activities may involve pre-screening of potential subjects over the telephone or in person is generally performed to determine their initial eligibility for, and, interest in a study and is a common strategy in the recruitment process.
Questions appropriate for pre-screening address the specific inclusion/exclusion criteria for the study and other issues of suitability, for example, an individual's ability to come to the research site multiple times.
It is not appropriate at this point in the process (i.e. prior to obtaining informed consent/enrollment) to gather information that is not directly related to assessing eligibility and suitability (e.g. obtaining complete medical histories, obtaining blood specimens for lab tests).
An additional telephone script is not required, for this pre-screening process, in addition to any scripts required under Recruitment question # 2.

Answer/Response: Yes

IF YES, submit any documents that will be used to collect pre-screening information so that the IRB may confirm what questions will be asked.
NOTE: To comply with HIPAA regulations only the minimum necessary information may be collected at this time. This means that only questions pertaining to the Inclusion and Exclusion Criteria may be asked.

IF YES,
DHHS: study team requests a Waiver of Documentation of Consent for Pre-screening questions.

HIPPA:
HIPAA does not apply if:
--no PHI is collected or

--if PHI is collected from a potential subject by an individual from a department that is not part of the HIPAA covered entity.

HIPAA does apply if the collection occurs by individuals* who work in a department that is part of the HIPAA covered entity.

In this case the collection will be covered under Health Care Operations/

These individuals are those that meet one of the following criteria:
--a UVa student working in the UVa HIPAA Covered Entity*
--a faculty or staff member in a PAID appointment in the UVA HIPAA Covered Entity*

**IF YES, Will any of the questions involve health information?**
Answer/Response: Yes

**IF YES, will you collect HIPAA identifiers with the health information?**
Answer/Response: No

**IF YES, which HIPAA identifiers will be recorded?**
Answer/Response:

**Do you confirm that health information with HIPAA identifiers will not be shared outside of UVa until a consent form is signed or only shared in a de-identified manner?**
Answer/Response:

4. **Do you plan to ask the subjects to do anything, other than answering questions, for the study prior to signing a consent?**

For example: come to the first visit fasting, stop taking medications that may be an exclusion criteria, change diet. As this is still part of pre-screening one is not allowed to gather information that is not directly related to inclusion/exclusion criteria or other issues of suitability (e.g. is person able to come to UVa for multiple visits)

NOTE:
Only those members of the study team with a DEA# (license to prescribe drugs) are allowed to determine if a potential subject may be asked/informed to stop taking a drug which is an exclusion criteria.
It is recommended that the potential subject notify their health care provider if they plan to stop a prescription drug.

Answer/Response: No

►**IF YES, explain in detail what you will ask them to do**.
Answer/Response:

Tips to Study Team
You must document their verbal consent in the study records.
If a subject is asked to stop taking a drug, document the date and name of the person on the study team giving the verbal order to stop medications (again- must be a person with a DEA#).

DHHS: Study team requests the use of Verbal Consent (Waiver of Documentation of Consent) for minimal risk screening procedures.

HIPPA:
If the individual, obtaining consent, works under the HIPAA Covered Entity this is covered under Health Care Operations
If the individual obtaining consent does not work under the HIPAA covered entity, HIPAA does not apply.

5. **How will the consenting process take place with either the prospective subject, the subject's legally authorized representative or parent/legal guardian of a minor ( if applicable)?**

HIPPA:
If the individual, obtaining consent, works under the HIPAA Covered Entity consenting is covered under Health Care Operations.

If the individual obtaining consent does not work under the HIPAA covered entity, HIPAA does not apply.

Describe the setting for the consent process.
If the study is of a sensitive nature and/or includes a reference to a medical condition how will you protect the privacy of the potential subject when they are approached to participate?
Who will discuss the study with the potential subject?
Where will the consenting process take place?
How will you assess subject understanding?
How much time will pass between obtaining written consent and initiation of study procedures?
See Protocol Examples: Consenting Process for examples of how to answer this question.
If recruiting minors, specify how parental /guardian consent will be obtained prior to approaching the minor.

Answer/Response:
After prospective study participant has made contact with a study investigator, they will be pre-screened to determine if they qualify for participation based on documented study inclusion/exclusion criteria. If they qualify, the study investigator will continue with the consent process by providing details about the study without giving emphasis to potential clinical benefits that may be associated with

participation. Since study participants will be randomly allocated to receive I.S. or EzPAP® therapy, researcher will explain the allocation process. They will then ask the potential study subject to demonstrate understanding of the study through verbal feedback. They will also be encouraged to ask clarifying questions.

**6. Will subjects sign a consent form for any part of the study?**

Answer/Response:

Yes. Subjects will be required to sign a consent form before they are enrolled into this study.

**7. Will the study procedures be started the same day the subject is recruited for the study?**

Answer/Response: Optional based on participant's desire and study investigator availability to conduct procedure and monitoring on the same day recruitment occurs.

**►IF YES, explain in detail why the subject cannot be given more time to make a decision to consent.**

Answer/Response: Prospective study participants will be granted time to consider whether they wish to accept invitation to enroll in this study.

**►IF YES, explain in detail what will be done to assure the potential subject has enough time to make an informed decision.**

Answer/Response: After reviewing the study protocol consent form with potential study subject, they will be reminded that they are not required to make a decision about participating in the study at that time. They will be directed to the primary study investigator's name and contact information as included in the study consent form. They will be advised to contact the study PI if they should decide to participate in the study at a later date.

**8. Is there the potential to recruit economically or educationally disadvantaged subjects, or other vulnerable subjects such as students or employees?**

**INSTRUCTIONS:** If you will be recruiting patients from the UVa Health System, you must answer this question YES as the UVa Health System cares for patients who are economically disadvantaged.

Answer/Response: Yes

**IF YES, what protections are in place to protect the rights and welfare of these subjects so that any possible coercion or undue influence is eliminated?**

Answer/Response:

Study investigators will review the study protocol with prospective participants and then ask for them to repeat, in their own words, their understanding of the study they are being invited to participate. Inability to follow verbal instructions is an exclusion criterion for study participation. Only study investigators will enroll study

participants. This study will require documentation of informed consent before study participation may occur. Study participants will be assured that nonparticipation will not affect routine medical care.

**9. Do you need to perform a "dry run" of any procedure outlined in this protocol?**

A "dry run" is a procedure done to validate the system used to obtain results. It requires a human "subject" however the results of the dry run are used for system validation and not for the actual research. A common example a "dry run" is the validation or qualification MRI scans required by sponsor to ensure the MRI at UVa is able to perform the study-required scans.

- **If you are doing a sponsored study that involves an MRI for research, you are encouraged to say YES to this question**
- If YES, complete and submit a Consent for a Dry Run Procedure
- A template for a Consent for Dry-Run MRI is located under FORMS on the IRB Website
- IF YES, answer the following questions.

Answer/Response: No.

**9a. List the "dry run" procedure(s) that must be performed.**
Answer/Response:

**9b. How many "subjects" will be recruited for "dry run" procedures?**
These "subjects" should NOT be counted with your total enrollment figures.
Answer/Response:

**9c. Describe the recruitment procedures for those participating in the "dry run".**
Answer/Response:

**9d. Will those participating in the "dry run" be compensated?**
IF YES, add the "dry run compensation" as a line item to the payment section of this protocol.
Answer/Response:

**9e. Who will pay for the cost of the "dry run" procedure(s)?**
Answer/Response:

**10. Is the study regulated by the Department of Defense (DoD)?**
Answer/Response: No

**If YES, do you confirm the following protections will be in place for military research participants to minimize undue influence?**
Answer/Response:

- Officers are not permitted to influence the decision of their subordinates.
- Officers and senior non-commissioned officers may not be present at the time of recruitment.
- Officers and senior non-commissioned officers have a separate opportunity to participate.
- When recruitment involves a percentage of a unit, an independent ombudsman is present.

**If YES, do you also confirm that the following procedures will be in place to require limitations on dual compensation?**
Answer/Response:

- Prohibit an individual from receiving pay of compensation for research during duty hours.
- An individual may be compensated for research if the participant is involved in the research when not on duty.
- Federal employees while on duty and non- federal persons may be compensated for blood draws for research up to $50 for each blood draw.
- Non-federal persons may be compensated for research participating other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

## Privacy Plan

**The following procedures must be followed.**

- The data will be secured per the Data Security Plan of this protocol.
- Only investigators for this study and clinicians caring for the patient will have access to data. They will each use a unique login ID and password that will keep confidential. The password should meet or exceed the standards described on the Information Technology Services (ITS) webpage about *The Importance of Choosing Strong Passwords.*
- Each investigator will sign the University's Electronic Access Agreement forward the signed agreement to the appropriate department as instructed on the form.

  If you currently have access to clinical data it is likely that you have already signed this form. You are not required to sign it again.
- UVa University Data Protection Standards will be followed http://www.virginia.edu/informationsecurity/dataprotection.
- If identifiable data is transferred to any other location such as a desktop, laptop, memory stick, CD etc. the researcher must follow the University's "Electronic Storage of Highly Sensitive Data Policy". Additional requirements may be found in the University's Requirements for Securing Electronic Devices.
- If identifiable data is taken away from the UVa Health System, Medical Center Policy # 0218 will be followed.

- Data will be securely removed from the server/drive, additional computer(s), and electronic media according to the University's Electronic Data Removal Policy.
- Data will be encrypted or removed if the electronic device is sent outside of UVa for repair according to the University's Electronic Data Removal Policy.
- If PHI will be faxed, researchers will follow the Health System Policy # 0194.
- If PHI will be emailed, researchers will follow the Health System Policy # 0193 and University Data Protection Standards .
- Data may not be analyzed for any other study without additional IRB approval.
- If you are using patient information you must follow Health System Policy # 0021.
- Both data on paper and stored electronically will follow the University's Record Management policy and the Commonwealth statute regarding the Destruction of Public Records.

***If you have a question or concerns about the required security standards contact ISPRO at it-security@virginia.edu***

**Summary of Requirements to Comply with UVa Health System, Medical Center and University Policies and Guidance as noted above:**

**Highly Sensitive Data** is:
-personal information that can lead to identity theft if exposed or
-data that reveals an individual's health condition and/or history of health services use.
**Protected Data (PHI)** a type of Highly Sensitive Data, is data combined with a HIPAA identifier
**Identifiable Data** under HIPAA regulations is considered to be *Highly Sensitive Data at UVa.*
A **Limited Data Set** (LDS) under HIPAA regulations is considered to be *Moderately Sensitive Data* at UVa.
The only HIPAA identifiers associated with data: dates and or postal address information limited to town or city, state, and zip code.
Will not include subjects age if older than 89 or subjects DOB if older than 89.

| **Highly Sensitive Data (Identifiable Health Info per HIPAA )** | **Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)** |
|---|---|
| *General Issues* | *General Issues* |
| Discussions in private<br>Do not share with those not on the study team or those who do not have a need to know. | Do not share with those not on the study team or those who do not have a need to know |
| Password protect | Password protect |
| Physically secure (lock) hard copies at all times if not directly supervised.<br>If not supervised hard copies must have double protection (e.g. lock on room OR cabinet AND in building requiring swipe card for entrance). | Physically secure (lock) hard copies at all times if not directly supervised. |
| For electronic documents turn off File Sharing; turn on firewalls; use up to date antivirus and antispyware; delete data securely. | For electronic documents turn off File Sharing; turn on firewalls; use up to date antivirus and antispyware; delete data securely. |
| Encrypt<br>See Encryption Solutions Guidance<br>*Files on Health System Network drives are automatically encrypted. If not stored there it is study teams responsibility to make sure data are encrypted.* | |
| If device sent out for service or repair, encrypt or remove data AND contract for repair using a UVa Purchase order. | If device sent out for service or repair, encrypt or remove data AND contract for repair using a UVa Purchase order. |
| Store files on a network drive specifically designated for storing this type of data, e.g. high-level security server/drives managed by Information Technology Services or the "F" and "O" managed by Heath Systems Computing Services. You may access it via a shortcut icon on your desktop, but you are not allowed to take it off line to a local drive such as the desktop of your computer (e.g. C drive) or to an individual Use Device*. May access via VPN | |
| Do not share with sponsor or other outside group before consent is obtained or the IRB has granted appropriate approvals and contract/ MTA is in place | Do not share with sponsor or other outside group before consent is obtained or the IRB has granted appropriate approvals and contract/ MTA is in place |
| If collected without consent/ HIPAA authorization will NOT be allowed to leave UVa HIPAA covered entity unless disclosure is approved by the IRB and the disclosure is tracked in EPIC | If collected without consent/ HIPAA authorization will NOT be allowed to leave UVa HIPAA covered entity unless disclosure is approved by the IRB and an MTA is in place prior to sharing of data |

| **Highly Sensitive Data (Identifiable Health Info per HIPAA )** | **Moderately Sensitive Data (Limited Data Set and De-identified data per HIPAA)** |
|---|---|
| *Electronic Data Collection & Sharing* | *Electronic Data Collection & Sharing* |
| (e.g. smart phone app, electronic consent using tablet etc.)<br>MUST consult with ISPRO or Health System Web Development Office: 434-243-6702<br>▪ University Side: IT-Security@virginia.edu<br>▪ Health System: Web Development Center: | |
| *Individual-Use Device* | *Individual-Use Device* |
| Do not save to individual-use device* without written approval of your Department AND VP or Dean.<br>If approval obtained, data must be password protected and encrypted. | |
| Do not save an email attachment containing HSD to an individual use device<br>( e.g. smart phone) | |
| *E Mail* | *E Mail* |
| Do not share via email with Outlook Web/ or forward email using other email vendors like Gmail/ Yahoo | |
| Do not send via email on smart phone unless phone is set up by Health System | |
| Email may include name, medical record number or Social Security number only if sending email to or from a person with * HS in their email address.<br>*NOTE: VPR & IRB staff do not meet this criteria!* | In addition to sharing LDS, may include initials if persons sending and receiving email work within the UVa HIPAA covered entity.** |
| *FAX* | *FAX* |
| Verify FAX number before faxing | Verify FAX number before faxing |
| Use Fax Cover Sheet with Confidentiality Statement | Use Fax Cover Sheet with Confidentiality Statement |
| Verify receiving fax machine is in a restricted access area | Verify receiving fax machine is in a restricted access area |
| Verify intended recipient is clearly indicated | Verify intended recipient is clearly indicated |
| Recipient is alerted to the pending transmission and is available to pick it up immediately | Recipient is alerted to the pending transmission and is available to pick it up immediately |

| **Highly Sensitive Data** | **Moderately Sensitive Data** |
|---|---|

| **(Identifiable Health Info Per HIPAA** | **(Limited Data Set and Deidentified data per HIPAA** |
|---|---|
| *Electronic Data Collection & Sharing* | *Electronic Data Collection & Sharing* |
| (e.g. smart phone app, electronic consent using tablet etc…)<br>MUST consult with ISPRO or Health System Web Development Office: 434-243-6702<br>University Side: IT-Security@virginia.edu<br>Health System: Web Development Center:<br>Contract must include required security measures. | |
| May be Stored in Qualtrics<br>MAY NOT be stored in places like UVaBOX, UVa Collab or QuestionPro<br>May also NOT be stored I n non-UVA licensed cloud providers, such as Dropbox, Google Drive, SkyDrive, Survey Monkey etc.. | May be stored in places like UVaBox, UVaCollab, Qualtrics<br>May NOT be stored in non-UVa licensed cloud providers, such as Dropbox, Google Drive, SkyDrive, Survey Monkey, etc. |
| *LOST OR STOLEN* | *LOST OR STOLEN* |
| Must report in accordance with protocol in accordance with the Information Security Incident Reporting Policy<br>Any data breach will also be reported to the IRB of record in the report meets the criteria of an Unanticipated Problem | Must report in accordance with protocol/ in accordance with the Information Security Incident Reporting Policy.<br><br>Any data breach will also be reported to the IRB of Record if the report meets the criteria of an Unanticipated Problem. |

** Individual Use Device – examples include smart phone, CD, flash (thumb) drive, laptop, C drive of your computer,*
***The UVa HIPAA covered entity is composed of the UVa VP Office of Research, the Health System, School of Medicine, School of Nursing, Nutrition Services (Morrison's), the Sheila C. Johnson Center, the Exercise and Sports Injury Laboratory and the Exercise Physiology Laboratory.*