Abbreviated Title: Wearable Incentive Spirometry

NIH IRB #: IRB001915

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Title: Feasibility of Measuring Volume of Inspiration Via Non-Invasive Motion Sensors

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STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812)

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; an IRB determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

PROTOCOL SUMMARY

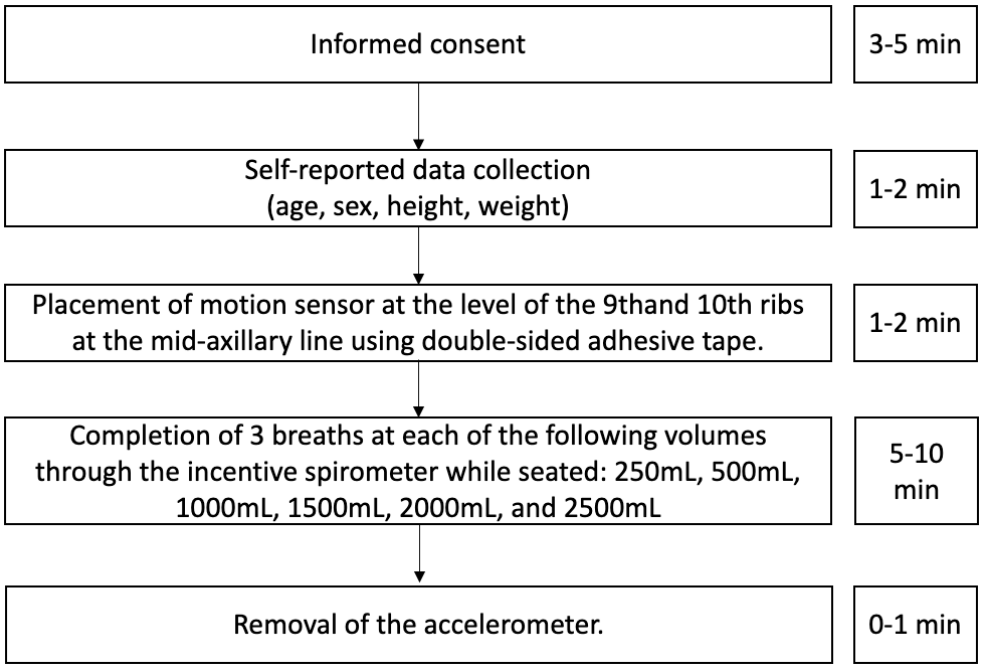
1.1 SYNOPSIS

Title:	Feasibility of Measuring Volume of Inspiration Via Non-Invasive Motion Sensors
Study Description:	This protocol is a basic physiologic proof-of-concept study enrolling normal volunteers to determine the feasibility of measuring volume of inspiration from chest wall motion measured via non-invasive thoracic motion sensors. The motion sensors are not medical devices because they are not intended to diagnose a disease or condition or to cure, mitigate, treat or prevent disease. Since motion sensors are not being evaluated for diagnostic purposes or being studied themselves within the context of this protocol and are only intended to collect physiological data, they are not to be considered investigational. The data collected in this feasibility study will not contain any personally identifiable information (PII). In this study, healthy participants will complete a total of approximately 18 measured breaths through a traditional incentive spirometer while wearing small, non-invasive motion sensors on their thorax at approximately the level of the 9th and 10th ribs unilaterally or bilaterally. The incentive spirometer is an FDA approved medical device. This study does not aim to study the safety or effectiveness of this device but rather utilize the device as a tool to measure volume of inspiration. The waveform data collected from the devices with each breath will then be analyzed with the intention to develop an algorithm that could convert chest wall motion to a discrete volume of inspiration in real time. Total enrollment time will be about 10-30 minutes per participant.
Objectives:	**Primary:** To collect chest wall motion data corresponding to various volumes of inspiration from a non-invasive wearable device. **Secondary:** To develop an algorithm which can convert chest wall motion to volume of inspiration and assess the algorithm using cross-validation strategy.
Endpoints:	**Primary:** A database of motion waveforms corresponding to each measured volume of inspiration via traditional incentive spirometer. **Secondary:** A cross-validated algorithm that converts chest wall motion to volume of inspiration.
Study Population:	Healthy volunteers of both sex and demographic groups who are ages 18 and older.

Description of Sites/Facilities Enrolling Participants:	All participants will be healthy volunteers recruited at the NIH.
Study Duration:	1 month
Participant Duration:	15-30 minutes

1.2 SCHEMA

Participation Flow Diagram



Flow diagram alt text:

1. Participants will be consented at the start of the meeting and provided a study ID to ensure patient confidentiality.
2. Each participant will then fill out a form with their study ID, age, sex, height, weight.
3. The small motion sensor will then be placed unilaterally or bilaterally on the patient's thorax at approximately the level of the 9^{th} and 10^{th} ribs at the mid-axillary line using hypoallergenic double-sided adhesive tape.
4. With the motion sensor is in place, the participant will then take breaths through a traditional FDA approved incentive spirometer. They will ideally complete three breaths at each of the following volumes: 250mL, 500mL, 1000mL, 1500mL, 2000mL, and 2500mL.
5. Upon completion, the motion sensor will be removed, and the participant will be free to go with no future scheduled appointments or follow-up.

INTRODUCTION

1.3 STUDY BACKGROUND AND RATIONALE

Postoperative pulmonary complications (PPCs) encompass a broad and heterogenous spectrum of conditions which serve as a leading cause of suboptimal surgical outcomes globally. Approximately 10-20% of the 310 million patients undergoing surgery each year will develop a PPC [1-6], and up to 25% of all deaths occurring within one week post-operatively attributed to PPCs [4]. These pulmonary complications, which range from minor respiratory alterations to severe conditions like pneumonia or respiratory failure, are a culmination of changes to the respiratory system that begin immediately after induction of general anesthesia. While under general anesthesia, patients experience decreased respiratory drive, reduced lung volumes, and altered ventilation perfusion relationship. The addition of a neuromuscular blocking drug for general anesthesia further increases risk for PPC with up to 75% of patients developing some degree of atelectasis post-operatively [7, 8]. The pain and fatigue many patients encounter post-operatively amplify the risk of PPCs, as patients become more hesitant to take deep, lung-expanding breaths. Considering these elements, it stands to reason that PPCs substantially influence prolonged hospital stays, elevated healthcare expenditures, and a deterioration in holistic patient outcomes.

Incentive spirometry (IS) has traditionally served as a cornerstone in the prophylaxis and management of PPCs. The incentive spirometer works by emulating a natural deep breath, serving simply as a visual tool for both patients and providers to gauge the quality and depth of lung expansion. The device does not offer any added resistance to assist in alveoli opening. By promoting voluntary deep breathing, the device helps to improve pulmonary function, maintain alveolar inflation, and enhance the clearance of secretions [9-11]. Despite its widespread acceptance in clinical practice, recent literature has shed light on various limitations associated with conventional incentive spirometry [12, 13]. Some of these drawbacks include patient compliance, nursing burden, and the lack of data storage for longitudinal tracking. Without a means to quantitatively assess patient effort and progress, it becomes difficult to assess the true impact of incentive spirometry on patient outcomes.

The continual advancements of digital health technologies and artificial intelligence present a compelling opportunity to address these gaps. Some efforts have been made by other groups to correlate chest wall motion with lung function, particularly in the asthma and apnea monitoring spaces. One group was successful in measuring respiration rate and lung volume using wearable strain sensors on a small cohort of volunteers. Others have detected respiratory rate via acoustic adhesive sensors on the neck [14] or detected changes in respiratory effort during sleep via an elastic band around the thorax and corresponding sensor measuring stretch patterns [15]. It is possible that we might identify unique patterns in chest wall motion via motion sensors adhered to the patient's thorax to easily measure and track volume of inspiration and respiratory effort post-operatively. This technology could open a door to improved IS compliance and may result in decreased nursing burden and improved post-operative management. If successful, it is possible that a wearable motion sensor could serve as a substitute for incentive spirometry with features to improve patient compliance, facilitate longitudinal IS data collection, and reduce burden on nursing staff who continuously have to provide incentive spirometers and remind patients to use them.

1.4 RISK/BENEFIT ASSESSMENT

1.4.1 Known Potential Risks

There only known risk to the participant is the development of a skin reaction or allergy to the hypoallergenic double-sided tape. Participants included in this study will be screened and excluded for known allergies to adhesives to mitigate this risk.

1.4.2 Known Potential Benefits

This study may not benefit specific study participants, but the results may help the investigators learn about the use of motion sensors to improve recording and tracking of post-operative incentive spirometry exercises and may potentially aid in post-operative management of future patients.

1.4.3 Assessment of Potential Risks and Benefits

The potential knowledge that may result from this study is considerable and may balance any potential risks to the participants. Proving that it is possible to detect volume of inspiration and respiratory rate from a non-invasive, wearable motion sensor could inform future studies which might work to improve IS compliance, data transmission, longitudinal tracking, and nursing burden.

OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To collect chest wall motion data corresponding to various volumes of inspiration from a non-invasive wearable device.	A database of motion waveforms corresponding to each measured volume of inspiration via traditional incentive spirometer.	The primary goal of this study is to collect data to correlate changes in chest wall motion with volume of inspiration. The first step in doing so is the creation of a database with this information.
Secondary		
To develop an algorithm which can convert chest wall motion to volume of inspiration and assess the algorithm using cross-validation strategy.	A cross-validated algorithm that converts chest wall motion to volume of inspiration.	This endpoint will allow us to prove the ability to calculate volume of inspiration from chest wall motion and assess its accuracy.

STUDY DESIGN

1.5 OVERALL DESIGN

Healthy volunteers (n = 30) will be recruited for participation in this proof-of-concept study. Each participant will be consented and assigned a study number to ensure that all data is non-PII. Participants will be asked to fill out a de-identified form with their age, sex, height and weight prior to application of motion sensor (see section **1.6**).

Each participant will wear the devices for approximately 10-30 minutes while they perform a series of breathing exercises. The thoracic wearable will be adhered unilaterally or bilaterally at approximately the level of the 9^{th} and 10^{th} ribs at the mid-axillary line. Hypoallergenic double-sided tape will be used to adhere the motion sensor to the volunteers' torso in this position. The participant will ideally take three breaths through a traditional incentive spirometer while wearing the devices at each of the following volumes: 250mL, 500mL, 1000mL, 1500mL, 2000mL, and 2500mL. Each breath will be held for approximately 5 seconds before being released. Throughout this period, the thoracic wearable will be detecting chest wall expansion. All data will be transmitted to a secure server located within the NIH clinical center for analysis and model creation. Upon completion of the breathing exercises, the device will be removed from the participant, and the participant will be free to leave. There will be no further study visits or contact required.

1.6 SCIENTIFIC RATIONALE FOR STUDY DESIGN

This is a basic physiologic proof-of-concept study to determine the feasibility of using a motion sensor to indirectly measure volume of inspiration. As such, there is no control group. The study design is appropriate to meet the goals of this study which are to acquire motion data from people taking measured breaths through traditional incentive spirometer.

1.7 JUSTIFICATION FOR INTERVENTION

The entire duration of study participation is 10-30 minutes, making this an incredibly low-commitment study for healthy volunteers. Minimum acceptable study participation is completion of the demographic information at least one attempt of all measured lung volumes, as it is possible that some participants will not be capable of taking the maximal volume of inspiration.

1.8 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed the demographic form and attempted all volumes of inspiration with the motion sensor in place.

Should the results of this basic physiologic proof-of-concept study be successful, future analysis of the technology developed (algorithm) would be submitted under a new IDE protocol to perform a study on a larger scale using this device and the algorithm which would be developed and marketed to assist in diagnosis, likely be considered a medical device at that time beholden to 21 CFR 812, used off label and likely would be NSR along with the algorithm that is developed.

1.9 DEVICE INFORMATION

1.9.1 Motion Sensor - 10-axis Bluetooth Gyro Inclinometer

The motion sensor is the "10-axis Bluetooth Gyro Inclinometer" by Wit Motion and is marketed for "rehabilitation exercises, workplace injury prevention, patient care, and healthy shortrange wireless motion measurements." The sensor is 2.02"x1.41"x0.59" and contains a rechargeable 3.7V Li-batter with a working time of approximately 4 hours. The casing is "indoor/outdoor, waterproof, dustproof, anti-UV and vibration resistant." The data output includes 3 axis (acceleration, gyro, angle, magnetic, and quaternion) and 1-axis barometer, air pressure, height data. Data is transmitted via Bluetooth 2.0. The device is not being studied for safety and effectiveness but is, rather, a tool for collecting basic physiologic data.

1.9.2 Incentive Spirometer - Teleflex Medical

An incentive spirometer is a device that measures the volume of the air inhaled into the lungs during inspiration. When breathing in through a volume-oriented incentive spirometer, a piston rises inside the device and measures the volume of the inspired air. The incentive spirometry device is widely used in physical, speech, and respiratory therapy as it encourages the patient to perform a slow and deep inspiration through visual feedback.[16] The incentive spirometer is FDA approved and will be used on label to collect physiological data and not evaluated for safety and efficacy or diagnostic purposes in support of labeling changes. The specific spirometer used for this study is the Hudson RCI 2500 VOLDYNE Volumetric Exerciser (REF 8884719011) manufactured by Teleflex Medical (Morrisville, NC USA).

STUDY POPULATION

1.10 INCLUSION CRITERIA

In order to be eligible to participate in this proof-of-concept study, an individual must meet all the following criteria:

1. Provision of signed and dated informed consent form.
2. Stated willingness to comply with all study procedures and availability for the duration of the study.
3. Male or female sex, aged 18-100
4. Ability of subject to understand and the willingness to sign a written informed consent document.

1.11 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Pregnancy.
2. Known allergic reactions to adhesive.
3. Patients with an altered mental status that precludes understanding and consenting for the procedure and compliance with the study activities.
4. Patients with known pulmonary conditions including pulmonary fibrosis, asthma, COPD, or chronic bronchitis.

1.12 INCLUSION OF VULNERABLE PARTICIPANTS

The study is designed to recruit healthy volunteers and we will not be including incapacitated adults.

1.12.1 Participation of NIH Staff or family members of study team members

NIH staff and family members of study team members may be enrolled in this study as this population meets the study entry criteria. NIH staff will not be recruited by their principal investigator or superior. Neither participation nor refusal to participate as a subject in the research will have an effect, either beneficial or adverse, on the participant's employment or position at NIH.

Every effort will be made to protect participant information, but such information may be available in medical records and may be available to authorized users outside of the study team in both an identifiable an unidentifiable manner.

The *NIH Frequently Asked Questions (FAQs) for Staff Who are Considering Participation in NIH Research* will be made available. Please see section **1.34.3** for consent of NIH Staff.

1.13 INCLUSION OF PREGNANT WOMEN, FETUSES OR NEONATES

This study will not include pregnant women. Women will be screened verbally for pregnancy and asked to sign a clause on the consent document attesting to being not pregnant. Pregnancy causes changes in breathing given added pressure on abdomen + diaphragm. As such, their data would likely skew data analysis with an N=30.

1.14 LIFESTYLE CONSIDERATIONS

Not applicable.

1.15 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened. Rescreened participants should be assigned the same participant number as for the initial screening.

1.16 STRATEGIES FOR RECRUITMENT AND RETENTION

Healthy adults of both sex, races, and ethnicities at the NIH will be recruited for participation in the study. The NIH will be the only study site included. We anticipate recruitment of approximately 30 volunteers. Volunteers will be made aware of this study through word of mouth and through the assistance from the Office of Patient Recruitment. Peer recruitment is proposed as an optimal method for our preliminary proof-of-concept study on the basic physiology of breathing given its small scale, lack of PII, short duration, and lack of invasive procedures. More robust recruitment of a broader population could be accomplished under a

future protocol if the findings of this proof-of-concept study is successful. Recruitment will be conducted on a peer-to-peer level with no individuals being recruited by an individual at a higher level of authority. Additionally, all peer recruiting activities will be structured to safeguard against risks such as undue pressure or the accidental disclosure of private health information, ensuring the protection and voluntary participation of all involved.

1.16.1 Costs

There will be no cost associated with participation.

1.16.2 Compensation

No compensation will be provided to the subjects. Research results will be made publicly available at the conclusion of this study.

STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

1.17 Study Interventions(s) or Experimental Manipulations(s) Administration

1.17.1 Study Intervention or Experimental Manipulation Description

All participants will be included in the interventional or experimental group for this study. There is no control group. The intervention includes the application of a small motion sensor placed on the patient's chest at approximately the level of the 9^{th} and 10^{th} ribs at approximately the mid-axillary line using hypoallergenic double-sided adhesive tape. With the motion sensor in place, the participant will then take breaths through a traditional FDA approved incentive spirometer. They will ideally complete three breaths at each of the following volumes: 250mL, 500mL, 750mL, 1000mL, 1500mL, 2000mL, and 2500mL. Upon completion, the motion sensor will be removed, and the participant will be free to go with no future scheduled appointments or follow-up.

1.17.2 Administration

Refer to section **1.17.1** for more details.

1.18 Fidelity

1.18.1 Interventionist Training and Tracking

N/A.

1.19 Measures to Minimize Bias: Randomization and Blinding

Participants will not be randomized or blinded for this proof-of-concept study.

1.20 Study Intervention/Experimental Manipulation Adherence

N/A.

1.21 Concomitant Therapy

Not applicable.

1.21.1 Rescue Therapy

N/A

STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

1.22 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Given the nature and design of this study (lasting approximately 10-30 minutes), discontinuation from the study intervention (the motion sensor) will mean discontinuation from the study. If any partial motion data or recorded demographic data have been collected prior to decision to discontinue the intervention, it will be shredded or deleted.

1.23 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- If the participant repeatedly fails to show up to their appointment
- Screen Failure

The reason for participant discontinuation or withdrawal from the study will be recorded on the Case Report Form (CRF).

1.24 LOST TO FOLLOW-UP

There will be no follow-up associated with this study.

STUDY ASSESSMENTS AND PROCEDURES

1.25 SCREENING PROCEDURES

1.25.1 Screening activities performed prior to obtaining informed consent

Minimal risk activities that may be performed before the subject has signed a consent include the following:

- Email, written, in person or telephone communications with prospective subjects.

1.25.2 Screening activities performed after a consent for screening has been signed

N/A

1.26 STUDY EVALUATIONS & PROCEDURES

All patients consented for participation will undergo the following procedures:

1. Recording self-reported age, sex, height, and weight.
2. Application of the motion sensor using a medical grade double sided adhesive.
3. While seated, each participant will ideally take three breaths at each of the following volumes through a traditional FDA approved incentive spirometer: 250mL, 500mL, 1000mL, 1500mL, 2000mL, and 2500mL. The participants will hold each breath for approximately 5 seconds before exhaling.
4. Data collection will include motion data transmitted from the motion sensor to a secure NIH server.

None of this data will be transmitted back to the participants themselves. All findings associated with this study will, however, be made publicly available upon the completion of this study.

1.26.1 Biospecimen Evaluations

N/A.

1.26.2 Samples for Genetic/Genomic Analysis

N.A.

1.27 Safety Assessments

All participants will be verbally screened for pregnancy and a history of skin allergy to adhesives to reduce risk of adverse effects.

1.28 Adverse Events and Serious Adverse Events

1.28.1 Definition of Adverse Event

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

1.28.2 Definition of Serious Adverse Events (SAE)

An adverse event or suspected adverse reaction is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

1.28.3 Classification of an Adverse Event

1.28.3.1 Severity of Event

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating. Of note, the term "severe" does not necessarily equate to "serious".]

1.28.3.2 Relationship to Study Intervention/Experimental Manipulation

All adverse events (AEs) will have their relationship to study procedures, including the intervention, assessed by an appropriately trained clinician based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

Related – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.

Not Related – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

1.28.3.3 Expectedness

A clinician with appropriate expertise in allergic dermatitis will be responsible for determining whether an adverse event is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

1.28.4 Time Period and Frequency for Event Assessment and Follow-Up

The occurrence of an adverse event or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

All AEs, not otherwise precluded per the protocol, will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

The research coordinator will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

1.28.5 Adverse Event Reporting

In consultation with the PI, a trained member of the study team will be responsible for conducting an evaluation of all adverse events and shall report the results of such evaluation to the NIH Institutional Review Board (IRB) as per Policy 801.

1.28.6 Serious Adverse Event Reporting

In consultation with the PI, a trained member of the study team will be responsible for conducting an evaluation of a serious adverse event and shall report the results of such evaluation to the Sponsor and the NIH Institutional Review Board (IRB) as per Policy 801.

1.28.7 Events of Special Interest

N/A.

1.28.8 Reporting of Pregnancy

N/A.

1.29 Unanticipated Problems

1.29.1 Definition of Unanticipated Problems

Any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied; and
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others (which many include research staff, family members or other individuals not directly participating in the research) at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or expected.

1.29.2 Unanticipated Problem Reporting

The investigator will report unanticipated problems (UPs) to the NIH Institutional Review Board (IRB) as per Policy 801.

STATISTICAL CONSIDERATIONS

1.30 Statistical Hypothesis

- Primary Endpoint Hypothesis: We will be able to transmit waveform data corresponding to each breathing exercise from the wearable motion sensor to the secure NIH database.
- Secondary Endpoint Hypothesis: Chest wall motion harnessed by a wearable motion sensor can be accurately converted to volume of inspiration.

1.31 Sample Size Determination

We hope to recruit approximately 30 participants for initial proof-of-concept data collection.

1.32 POPULATIONS FOR ANALYSES

All participants will be analyzed via a per-protocol analysis. This method defines a subset of the participants in the full analysis (ITT) set who complied with the protocol sufficiently to ensure that these data would be likely to a) result in accurate models to predict post-operative outcomes, and b) represent the effects of the wearable on post-operative outcomes.

1.33 STATISTICAL ANALYSES

1.33.1 General Approach

Data will be transmitted from the motion sensors to a secure NIH server for storage. Motion data will be quality checked and corrupted waveforms will be removed. Waveforms corresponding to activity (motion artifacts) will also be removed, per standard signal processing techniques. The waveforms will then be parsed out by corresponding volume of inspiration. A customized model will be fine-tuned on these sequences, learning to recognize patterns in chest wall motion associated with each incentive lung volume. To ensure that the model is unbiased, class balancing will be performed for both demographic and clinical labels using majority under-sampling techniques. The transformer model will be fine-tuned and validated on the subjects in the dataset. Once the model is fully developed from the data collected in this study, we will test it against the traditional incentive spirometry to calculate its accuracy.

1.33.2 Analysis of the Primary Endpoints

Primary Endpoint: A database of motion waveforms corresponding to each measured volume of inspiration via traditional incentive spirometer.

This endpoint will be deemed successfully completed once the data has been transmitted from the motion sensor to the secure NIH server for all participants. The primary goal of this study is to collect waveform data to correlate changes in chest wall motion with volume of inspiration. The first step in doing so is creation of a database with this information. All motion data will be quality checked and corrupted waveforms will be removed. Waveforms corresponding to activity will also be removed, per standard signal processing techniques.

1.33.3 Analysis of the Secondary Endpoint(s)

Secondary Endpoint: A cross-validated algorithm that converts chest wall motion to volume of inspiration.

Motion waveforms will be annotated by volume of inspiration. A model will be fine-tuned on these sequences, learning to recognize subtle deteriorations in the waveform that correspond with varying volumes of inspiration. The pre-trained AI models will be validated for each task (e.g., each measured volume of inspiration). This will be done using a validation set and then test using a held-out test set wherein no parameter optimization is performed. Different validation and test sets will be generated using a cross-validation strategy such as stratified K-fold.

1.33.4 Safety Analyses

N/A.

1.33.5 Sub-Group Analyses

Results will be analyzed as a whole and then based on sex and BMI to determine if these factors significantly impact chest wall motion corresponding to teach volume of inspiration.

1.33.6 Tabulation of individual Participant Data

De-identified participant data will be listed by measure and time point within our secure database; however, all data will be analyzed and presented as a group for further presentation or publication.

1.33.7 Exploratory Analyses

N/A.

REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

1.34 INFORMED CONSENT PROCESS

1.34.1 Consent Procedures and Documentation

Informed consent will be obtained at the start of the investigational appointment (10-30 minutes in length) with the principal investigator, or an associate investigator listed on the protocol. This meeting will take place in a quiet, private patient room with a closed door with only relevant parties present. The risks and benefits of the procedure and the study will be discussed with the participant. Ample time will be given for the participant to ask questions, and all questions will be completely answered by the principal investigator or the associate investigator during the consent process. Once informed consent is obtained, the form will be labeled with a unique study identification number. This unique ID will be used to make all further data collection de-identified. The consent forms will be sent to the NIH Health Information Management Department who will make it available in a digital form in the CRIS electronic medical record.

1.34.2 Consent Process by Telephone/NIH-Approved Telehealth Platform/iMED

Informed consent will be obtained per the Clinical Center Policy and Communication Bulletin MAS policy M20-1 and IRB Policy 303. Subjects will be provided a copy of the consent for review. Subjects will be given ample time to read and review the consent before the appointment for the formal informed consent process and signing. Subjects will choose the location for the telephone/telehealth informed consent process, but the research team will highly encourage the subjects to choose a location that will private, quiet, and have the remote possibility of interruptions. Subjects will be contacted either by telephone or NIH-approved telehealth platform and the non-investigational nature of this trial, the associated assessment and test options, biological sample collection, and attendant risks and discomforts will be carefully explained to the subject.

The subject will sign and date either the paper informed consent or use electronic signature (e-sign) using the CC approved platform or method (iMED).

If electronic signatures will be used, the study team plans to use the CC approved platform, currently iMED consent, to obtain electronic signatures. The identity of participants will be verified by asking them to state their full name and date of birth. The electronic signatures will be obtained “synchronously and in real-time” whether it is in-person, telephone, or telehealth consent. iMED consent will capture electronic signatures via the methods listed below:

- Using a smartphone: participants will be registering their signatures using their finger. Participants will receive a secure link that leads them to secure "web pages" that will capture their electronic signatures using their finger.
- Using a computer/tablet/laptop: participants will be registering their signatures using a computer mouse or their finger/stylus (for touch/stylus enabled tablets and computer screens). Participants will receive a secure link that leads them to secure "web pages" that will capture their electronic signatures using the aforementioned methods.

Signed paper copies of consent will be returned via fax, mail, or secure e-mail to the consenting investigator to be signed and dated. A fully executed copy of the consent will be available in the participant's research record. Consent forms signed using the CC approved electronic signature platform (iMED consent) will be archived and stored in the participant's research record via an automatic secure electronic transmission immediately after all the required signatures are obtained. All participants will be provided with a copy of the fully executed consent (paper copy by mail or electronic copy by secure electronic methods based on participant's preference). The informed consent process will be documented in the medical record, including the name of the interpreter.

1.34.3 Considerations for Consent of NIH staff, or family members of study team members

Consent for NIH staff will be obtained as detailed above with following additional protections:

Consent from staff members will be obtained by an individual independent of the staff member's team whenever possible. If a staff member participates in the study, consent will not be obtained by the principal investigator or any direct superior on the research team. Otherwise, the consent procedure will be monitored by the CC Department of Bioethics Consultation Service in order to minimize the risk of undue pressure on the staff member.

The *NIH Frequently Asked Questions (FAQs) for Staff Who are Considering Participation in NIH Research* will be made available.

1.34.4 Consent of Subjects who Are, Or Become, Decisionally Impaired

Adults unable to provide consent are excluded from enrolling in the protocol. Given the short study duration (10-20 minutes), it is highly unlikely that participants would lose capacity to provide consent within the duration of the study.

1.35 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to study participants, investigator, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable

- Determination that the primary endpoint has been met

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the IRB.

1.36 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s). This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence.

All research activities will be conducted in as private a setting as possible.

The study monitor, representatives of the Institutional Review Board (IRB), and/or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's data will be securely stored for internal use and analysis during the study. At the end of the study, all records will continue to be saved digitally in the DRD shared drive managed by DCRI for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at a secure NIH server within the NIH Clinical Center building. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by clinical center research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived on a secure NIH server.

To further protect the privacy of study participants, a Certificate of Confidentiality has been issued by the National Institutes of Health (NIH). This certificate protects identifiable research information from forced disclosure. It allows the investigator and others who have access to research records to refuse to disclose identifying information on research participation in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. By protecting researchers and institutions from being compelled to disclose information that would identify research participants, Certificates of Confidentiality help achieve the research objectives and promote participation in studies by helping assure confidentiality and privacy to participants.

1.36.1 Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see https://grants.nih.gov/policy/sharing.htm). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be

thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

1.36.2 Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see https://humansubjects.nih.gov/coc/index). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the protocol is managed in compliance with Federal statutes, and regulations. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

1.37 Future use of Stored Specimens and Data

We do not intend to store any specimens for this protocol. All motion data will be stored through a secure NIH server located in the NIH Clinical Center.

1.38 Safety Oversight

Safety oversight will be performed through the NIH Clinical Center's Quality Assurance Program. The clinical research team will meet on a regular basis (approximately weekly) when subjects are being actively enrolled/evaluated on the study to discuss data analysis or operational issues.

All data will be collected in a timely manner and reviewed by the principal investigator or a lead associate investigator. Events meeting requirements for expedited reporting as described in HRPP Policy 801 will be submitted within the required timelines.

The principal investigator will review all data on each subject to ensure safety and data accuracy. The principal investigator will personally conduct or supervise the investigation and provide appropriate delegation of responsibilities to other members of the research staff.

1.39 Clinical Monitoring

Accrual and safety data will be monitored by the principal investigator, who will provide oversight to the conduct of this study. The PI will continuously evaluate implementation of the protocol for any unusual or unpredicted complications that occur and will review the data for accuracy and completeness. The principal investigator will review adverse event and response data on each patient to ensure safety and data accuracy. The principal investigator will personally conduct or supervise the investigation and provide appropriate delegation of responsibilities to other members of the research staff.

1.40 Quality Assurance and Quality Control

Each clinical site will perform internal quality management of study conduct, data and biological specimen collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management. The device will only have contact with the skin via the adhesive and will not be exposed to any bodily fluids. The casing is "indoor/outdoor, waterproof, dustproof, anti-UV and vibration resistant. It will be sanitized with a hydrogen peroxide cleaner disinfectant wipe between each use.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted, and data are generated and biological specimens are collected, documented (recorded), and reported in compliance with the protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements (e.g., Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP)).

The investigational site will provide direct access to all study related sites, source data/documents, and reports for the purpose of monitoring and auditing by the IC, and inspection by local and regulatory authorities.

1.41 Data Handling and Record Keeping

1.41.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the assigned study coordinator under the supervision of the principal investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All data in this study will be collected and stored digitally. Data will be entered into an Excel spreadsheet on the research NIH-owned computer during and after each procedure. The data will be transferred to a secure server in the DRD shared drive that is password protected and compliant with the data collection policies of the NIH Clinical Center and federal regulations for storage, analysis and archiving. All relevant data from the patient chart will also be entered on an encrypted private computer database from which formal analyses are done, according to NIH and Clinical Center policy. The secure central data base will be maintained by the data base manager on a secure password protected computer with secure Clinical Center network backup, in accordance with NIH CC policy. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. The responsible investigators are Peter Pinto, MD.

1.41.2 Study Records Retention

Study documents should be retained as per the NIH Intramural Records Retention Schedule. No records will be destroyed without the written consent of the sponsor, if applicable.

1.42 Protocol Deviations and Non-Compliance

It is the responsibility of the investigator to use continuous vigilance to identify and report deviations to the NIH Institutional Review Board as per Policy 801. All deviations must be

addressed in study source documents, reported to Clinical Center Program Official. The investigator is responsible for knowing and adhering to the reviewing IRB requirements.

1.42.1.1 NIH Definition of Protocol Deviation

A protocol deviation is any changed, divergence, or departure from the IRB-approved research protocol.

- Major deviations: Deviations from the IRB approved protocol that have, or may have the potential to, negatively impact the rights, welfare or safety of the subject, or to substantially negatively impact the scientific integrity or validity of the study.
- Minor deviations: Deviations that do not have the potential to negatively impact the rights, safety or welfare of subjects or others, or the scientific integrity or validity of the study.

1.43 HUMAN DATA SHARING AND PUBLICATION

This study will comply with the NIH Data Management and Sharing (DMS) Policy, which applies to all new and ongoing NIH-funded research in the IRP, as of January 25, 2023, that is associated with a ZIA, with a clinical protocol that undergoes scientific review.

1.43.1 NIH Public Access Policy Compliance

This study will comply with the NIH Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

ABBREVIATIONS

AE	Adverse Event
CFR	Code of Federal Regulations
CRF	Case Report Form
DCC	Data Coordinating Center
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
ICH	International Council on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IRB	Institutional Review Board
IS	Incentive Spirometry
ISM	Independent Safety Monitor
MOP	Manual of Procedures
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections

PI	Principal Investigator
PII	Personally Identifiable Information
PPC	Postoperative Pulmonary Complications
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

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