1. Cover Page

STUDY TITLE:	Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study
Study acronym:	The BENEFIT Study
PROTOCOL NUMBER:	18-BR-0001
VERSION:	2
DATE:	August 20, 2018

Revision History

Version	Description of Change
1	Initial release
1a	Administrative change to correct typos and clarify timing of chest X-ray following the procedure as requested by MUSC IRB (only MUSC)
2	Administrative change to clarify and resolve inconsistencies in the protocol and to conduct the study according to the unified protocol at all centers

Clinical Investigation Plan (CIP) and Protocol
Identification of Responsibility Page

Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study

The Study will be performed in accordance with the relevant parts of Title 21 CFR Parts 812, 50, 54, 56 and ISO 14155-1 / 14155-2.1; the ICH Guidelines for Good Clinical Practices (E6), the Declaration of Helsinki, and any regional and/or national regulations

Sponsor:	Auris Health, Inc. 125 Shoreline Dr Redwood City, CA 94065	Sponsor Contact: Scott Rehage Email: scott.rehage@aurishealth.com
Principal Investigators / Study Centers:	Listed in Appendix III	
Date of Issue:	August 20, 2018 Version 2	

This protocol contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. It should be held confidential and maintained in a secure location.

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Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study

Approval Page

STUDY TITLE:	Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study
PROTOCOL NUMBER:	18-BR-0001
VERSION NUMBER:	2
DATE:	August 20, 2018

We, the undersigned, have read and approve the protocol specified above and agree on its content.

Josh DeFonzo

Date:

Emir Deljkich

Date:

Joy Sacmar

Date:

Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study

Approval Page

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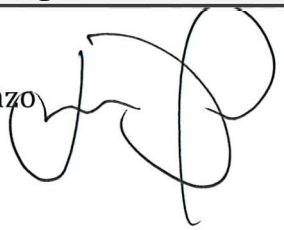
Josh DeFonzo



21 August 2018

Date:

Emir Deljkich

20 August, 2018

Date:

Joy Sacmar

21 August 2018

Date:

AURIS study – Investigator's Signature Page

STUDY TITLE: Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study

STUDY CENTER: <Insert Study Center, Location>

I, the undersigned, have read and understand the protocol specified above and agree on its content. I agree to perform and conduct the study as described in the protocol. In addition, when applicable, I agree to enlist sub-investigators who also agree to perform and conduct the study as described in the protocol.

_____

SITE PI – Print Name

_____

SITE PI – Signature

_____

DATE

1.1 Table of Contents

1.2 Amendment Change History

This is version 2 of the protocol.

1.3 Synopsis of Trial

Robotic Bronchoscopy for Peripheral Pulmonary Lesions: A Multicenter Pilot and Feasibility Study

Primary Objective	The objective of this study is to evaluate the feasibility of performing robotic navigation of peripheral airways in human subjects for the purpose of biopsying peripheral lung lesions.
Test Device	The Monarch Endoscopy Platform
Control Device	None
Indication for Use **510K #:** 173760	The Monarch Endoscopy Platform is FDA cleared medical device (**510K #: 173760)** intended to provide bronchoscopic visualization of and access to patient airways for diagnostic and therapeutic procedures. The system is intended to be used by qualified physicians only.
Hypotheses	No formal statistical hypotheses are defined. It is believed that the Monarch platform will be capable of enhancing access to peripheral lung lesions.
Study Design	A multi-center, prospective, single arm pilot and feasibility study to evaluate the use of a robotic endoscopic system to access and biopsy peripheral pulmonary lesions. The Monarch Endoscopy Platform will be used in conjunction with a navigational bronchoscopy with biopsy.
Number of Patients	The study will enroll up to 55 patients. It is expected that each center will enroll up to 11 study patients, of which the first patient may be considered roll-in patient and analyzed separately.
Sites	Investigational sites are listed in the Appendix III.
Duration of Study	For the purpose of the study, each enrolled subject will be followed up to 84-hours post procedure (a follow-up phone call will be made 24-84 hr post procedure). The enrollment will take up to 45 calendar days per center. The total duration of the study is expected to be up to 5 months.
Primary Effectiveness Endpoint	The primary effectiveness endpoint is the successful navigation to targeted peripheral pulmonary lesions sized 1-5cm as confirmed using radial probe endobronchial ultrasound (R-EBUS).

Secondary Effectiveness Endpoints	The following will be considered secondary endpoints: • Time to R-EBUS confirmation (lesion localization), time to the tissue acquisition confirmation, Total procedure time (from introduction to removal of the bronchoscope) and procedure interruptions • Radiographic and procedural factors that influence the ability to successfully navigate to peripheral lesions including size and location of peripheral lesions • Diagnostic yield • Conversion to conventional bronchoscopic procedure
Primary Safety Endpoint	Device or procedure related adverse events (AEs).
Secondary Safety Endpoint	Complications unrelated to device.
Follow-Up Schedule	Each enrolled subject will have one follow-up visit (phone call). The phone call will be made between 24-84 hours post-procedure. This window is established to accommodate patients undergoing the bronchoscopy procedure on Fridays.
Pre-Operative Inclusion Criteria	1. 18 to 80 years of age; 2. Capable and willing to give informed consent; 3. Acceptable candidate for an elective, non-emergent bronchoscopic procedure; 4. Solid peripheral lung lesions suspected of malignancy, between 1-5cm in size identified on thin slice CT scan within 14 days of the intended bronchoscopy 5. Lack bleeding disorders
Pre-Operative Exclusion Criteria	Subjects will be excluded from participating in this Study if they meet any of the following criteria prior to initiation of the endoscopic procedure: 1. Medical contraindication to bronchoscopy; 2. Patients with a subsolid nodule and/or ground-glass opacity lesions on pre-procedure chest CT 3. Patients with endobronchial involvement seen on chest CT 4. Lack fitness to undergo flexible bronchoscopy as determined by the bronchoscopist prior to procedure, and 5. Participation in any other investigational clinical trial (device or medication) 30 days before and throughout the duration of the study; 6. Uncontrolled or irreversible coagulopathy; 7. Female subjects who are pregnant or nursing or those of child-bearing potential refusing a pregnancy test; 8. Have significant mediastinal lymphadenopathy on chest CT scan and/or PET CT abnormalities suggestive of advanced stage lung cancer with mediastinal lymph node involvement
Intra-Procedure Exclusion Criteria	Any presenting condition discovered intra-procedurally that in the opinion of the investigator would make participating in this study not in the patient's best interest.
Study Sponsorship	
Sponsor	Auris Health, Inc 150 Shoreline Dr Redwood City, CA 94065

2. Introduction

Successful biopsy of peripheral pulmonary lesions remains a challenge due to a number of factors, one of which may be the ability to gain access to peripheral lesions due to the size and maneuverability of conventional bronchoscopes. In this study, we will evaluate the feasibility of a new technique using a robotic endoscope with navigational platform to both access and biopsy peripheral pulmonary lesions.

2.1 Background

Peripheral bronchoscopy is often performed to biopsy peripheral pulmonary lesions (PPL's) for diagnostic purposes. With the results of the National Lung Cancer Screening Trial demonstrating a 20% reduction in lung cancer related death, widespread adoption of lung cancer screening programs is expected to result in the detection of significantly increased numbers of pulmonary nodules[1]. While the majority of these nodules may simply require surveillance imaging, many will require biopsy.

Conventional bronchoscopic approaches to peripheral pulmonary lesions is typically performed using flexible bronchoscopes with outer diameters of 4 or 6 mm. The bronchoscope is inserted into the tracheobronchial tree and then is maneuvered into segmental and subsegmental bronchi by the bronchoscopist. Rotation and flexion of the bronchoscope is performed by the bronchoscopist who is responsible for "driving" the bronchoscope into peripheral airways.

Current limitations to using this approach include challenges advancing the bronchoscope into peripheral airways due to size limitations of conventional bronchoscopes as subsegmental bronchi become progressively smaller as they extend peripherally. In addition to this, subsegmental bronchi often branch at varying angles which often cannot be negotiated using conventional bronchoscopes. These factors may limit the bronchoscopist's ability to advance the bronchoscope into close proximity to peripheral pulmonary lesions when attempting biopsy, and this may negatively affect the diagnostic yield of the procedure.

Despite technological advancements in guided bronchoscopy such as electromagnetic navigation bronchoscopy and radial probe endobronchial ultrasound, the diagnostic yield of bronchoscopic approaches for peripheral lesions, particularly those smaller than 2cm, remains suboptimal, at less than 60%.[2,3,4]

Robotic surgery has been performed across many platforms including urologic, gynecologic and thoracic surgery, and offers potential advantages of improved dexterity and visualization while maintaining minimally invasive approaches[5]. Early experience using a robotic endoscopic system within human cadaveric lungs demonstrated increased reach into the lung periphery using the robotic platform compared with a similarly sized bronchoscope[6]. Presently, very little data exists regarding the use of a robotic endoscopic system in live human subjects with peripheral lesions in need of biopsy.

The Monarch platform is a "robotic" assisted or electromechanical, software driven endoscopy system designed to be used by qualified physicians to provide bronchoscopic visualization of and access to patient airways for diagnostic and therapeutic procedures. The system is intended to be used by qualified physicians only. FDA has cleared the Monarch platform under the 510(k)-clearance process (510K #: 173760).

The Monarch system has been extensively tested in porcine and cadaver studies. The system has been also tested in a clinical feasibility study to obtain lung biopsy specimens. Herein, we propose a multi-center, post-market, clinical trial to evaluate the feasibility of a new technique using a robotic endoscope with navigational platform to both access and biopsy peripheral pulmonary lesions.

Specific Risk and Benefits

Risks of procedures

With any bronchoscopic procedure, there is the possibility of the following risks: collapsed lung, pneumothorax, bronchoscopic airway puncture, breathing difficulty, vocal cord spasm, vomiting, dizziness, bronchial spasm, infection, low blood oxygen, feeling of heaviness in chest, heart attack and bleeding from biopsied site. The occurrence of these risks is extremely low. The measures to mitigate the risks are the same as for all bronchoscopy. To minimize the chance of bleeding, all patients will be questioned about tendency to bleed prior to bronchoscopy as per standard care. Anticoagulation with antiplatelet agents will be held according to guideline recommendations for that drug. If bleeding occurs, patients will be treated with direct pressure, local instillation of epinephrine or electrocautery. Vocal cord spasm will be prevented through the use of lidocaine on the vocal cords. Patients with lung disease may receive bronchodilators prior to bronchoscopy at the discretion of the performing bronchoscopist. There is no way to reduce the minimal risk of infection due to bronchoscopy since the scope must go through the naso or oropharynx. Patients are given supplemental oxygen and their oxygen level is continuously monitored using pulse oximetry. Patients ECG, heart rate, blood pressure, and blood oxygen are continuously monitored by a nurse, respiratory therapist and physician during the procedure. If there is any sign of a worsening in status, such as elevated heart rate, low oxygen, or ECG changes, the procedure will be aborted. In the event that any of these were to occur, the study subject will be treated for the condition. Some subjects may experience wheezing, coughing, or shortness of breath during the first few days following a bronchoscopy procedure.

The additional risks from bronchoscopy are related to anesthesia and the very act of intubation and passing a bronchoscope into the airway. To mitigate risks of bronchoscopy all patients will be monitored according to local guidelines for the type of anesthesia technique used according to standard of care. In addition, oxygen saturation (using pulse oximetry) respiratory rate, blood pressure, ECG, and heart rate will be

continuously monitored. Patients will not be released until they are fully awake and medically stable.

Anesthesia Risk

Typically, patients will be under general anesthesia during the procedure. This means that patients won't feel anything during intubation. Healthy people usually don't have any problems with general anesthesia, but there's a small risk of long-term complications. These risks largely depend on patients' general health and the type of procedure you're undergoing.

There is a potential risk of developing side effects associated with the use of anesthesia. The risks of anesthesia depend on the agents and/or gases used. The risks of anesthesia include postoperative pain, nausea and vomiting, dizziness, drowsiness, shivering, liver toxicity and/or cardiovascular events. Trained professionals with extensive experience and expertise who routinely administer general or local anesthesia with conscious sedation to patients requiring multiple procedures will be responsible for the induction and associate monitoring required for this study. In addition, study patients will undergo extensive monitoring throughout the recovery period.

Intubation Risk

With any intubation, there are some risks related to intubation, such as: injury to teeth or dental work, injury to the throat or trachea, a buildup of too much fluid in organs of tissues, bleeding, lung injury of complications and aspiration (stomach contents and acids that end up in the lung). Anesthesiologist or trained personnel will evaluate patients before the procedure to help decrease the risk of these complications from occurring. You'll also be monitored carefully throughout the procedure.

Risk Mitigation

Risks during study participation will be minimized by the following:

The study protocol was developed with investigators that is well-known in the area of interventional pulmonology. The sites were chosen because of proven expertise in the field of interventional pulmonology. All Investigators performing the procedure using the Monarch Endoscopy Platform under the clinical protocol will undergo a Training Program, which includes elements of both a didactic and training program. Proficiency must be demonstrated prior to use the Platform in humans. Pre-clinical, *in vitro* and *in vivo* testing has been performed in order to optimize the device safety and function.

Research only risks

Every effort will be made to protect the privacy of the research subjects. All information and data related to this study will be maintained in secured, protected space, and access will be restricted to study personnel only. In addition to this, additional procedure time

may be encountered due to the robotic assisted bronchoscopy procedure, particularly in cases where salvage procedures are performed.

Benefits

The primary potential benefit of participation is the occurrence of a successful biopsy of tissue for pathological evaluation which is necessary to support specific treatment. Results will be evaluated in this study and will further support the development of bronchoscopic equipment for pulmonary and thoracic physicians.

2.2 Purpose

The purpose of the trial is to evaluate the feasibility and safety of using the Monarch Endoscopy Platform to biopsy peripheral pulmonary lesions 1-5cm in size in eligible patients.

The Study will be performed in accordance with the relevant parts of Title 21 CFR Parts 812, 50, 54, 56 and ISO 14155-1 / 14155-2.1; the current versions of the ICH Guidelines for Good Clinical Practices, the Declaration of Helsinki, and any regional and/or national regulation.

3. Trial Objectives

Despite technical advancements in guided bronchoscopy, the diagnostic yield for peripheral pulmonary lesions remains suboptimal. One potential explanation for the suboptimal yield may be the inability to place the endoscope within close proximity of the targeted lesion. The Monarch Endoscopy Platform has demonstrated the ability to reach further into the periphery than a similarly sized conventional thin bronchoscope in human cadaveric lungs. The objective of this study is to evaluate the feasibility of performing robotic navigation of peripheral airways in live human subjects for the purpose of biopsying peripheral lung lesions.

4. Investigational Plan

4.1 Trial Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint is the successful navigation to targeted peripheral pulmonary lesions sized 1-5cm as confirmed using radial probe endobronchial ultrasound.

Secondary Effectiveness Endpoint

The following will be considered secondary endpoints:

- Time to R-EBUS confirmation (lesion localization)
- Time to the tissue acquisition confirmation
- Total procedure time (from introduction to removal of the bronchoscope) and procedure interruptions
- Radiographic and procedural factors that influence the ability to successfully navigate to peripheral lesions including size and location of peripheral lesions
- Diagnostic yield
- Conversion to conventional bronchoscopic procedure

Primary Safety Endpoint

Device or procedure related adverse events.

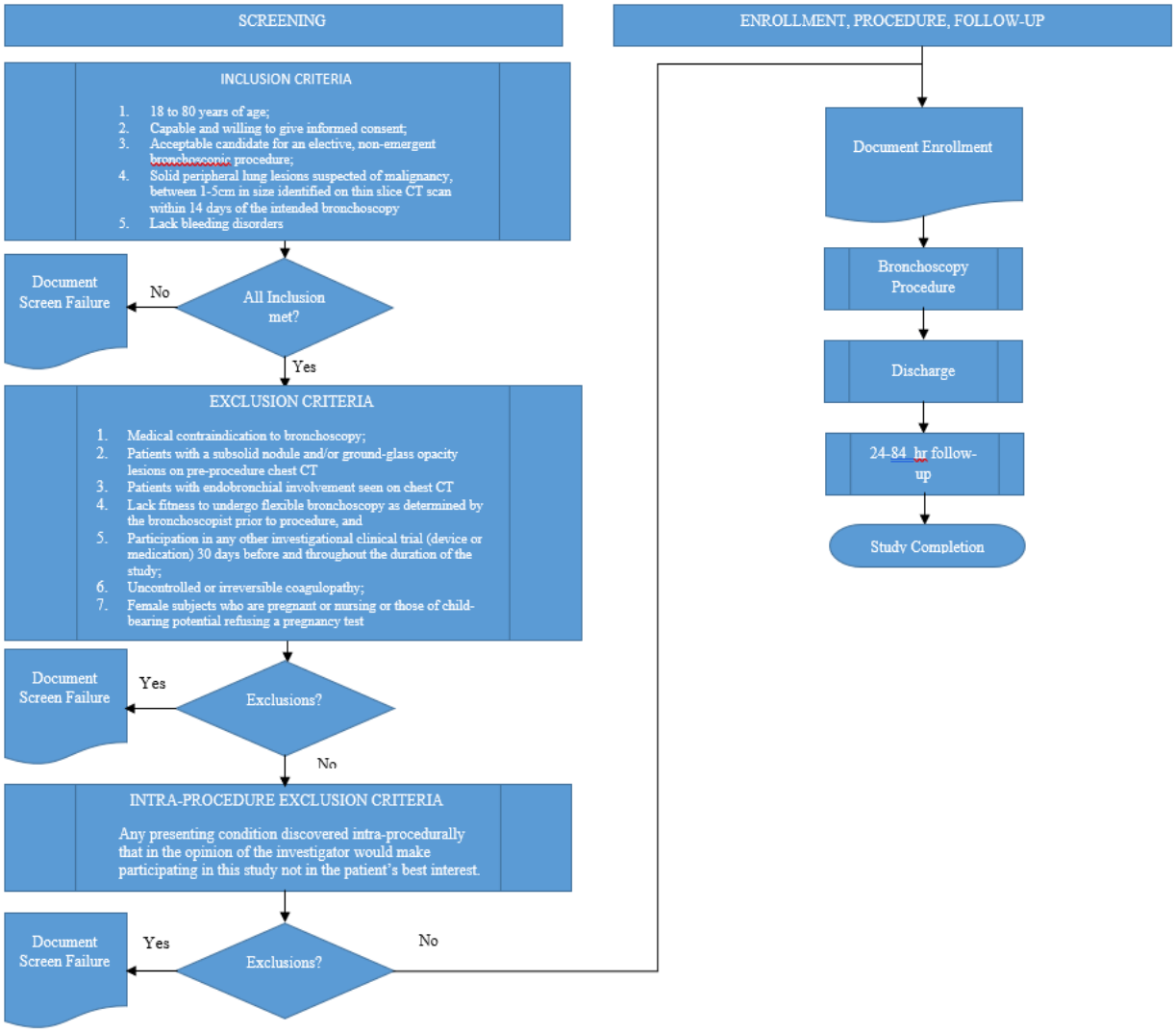
Secondary Safety Endpoint

Complications unrelated to device.

4.2 Trial Design

This is a prospective, multicenter, open-label pilot and feasibility study to evaluate the use of the Monarch Endoscopy Platform to access and biopsy peripheral pulmonary lesions. It is expected that up to 5 centers will participate in the trial. Subjects 18 years or older presenting with peripheral pulmonary lesions determined to require a non-surgical biopsy as per standard medical care and meet study inclusion and exclusion criteria will be invited to participate. Each site principle investigator will determine eligibility and will explain the study to qualified subjects prior to obtaining consent. The subject will also be given an opportunity to review and sign documentation of HIPAA compliance and authorization according to establish practice of the institutions. All subjects are required to meet the inclusion/exclusion criteria defined in the sections 5.1 and 5.2 in order to be considered eligible for participation in this Study. The study flowchart is shown in the Figure 1.

Figure 1. Schematic of Study Design.



Investigational Sites

The Investigational sites are listed in Appendix III.

Sample size

The study will enroll up to 55 patients. It is expected that each center will enroll up to 11 study patients, of which the first patient may be considered roll-in patient and analyzed separately. The enrollment will take up to 45 calendar days per center. The total duration of the study is expected to be up to 5 months. In case of slower than planned enrollment at individual trial sites, other sites may be permitted to enroll more patients.

Procedures

1. *Prior to bronchoscopy*: eligible patients will have had a thin slice CT of the chest performed as part of standard medical care within the preceding 14 days that will be available to review during procedures.

2. *Flexible bronchoscopy*: procedures will be performed in an operating room or dedicated endoscopy suite using either general anesthesia (typically) or moderate sedation. Following sufficient sedation, patients will be intubated using an endotracheal tube no smaller than 8mm. Flexible bronchoscopy will then be performed using the conventional standard of care bronchoscope used at the hospital for airway inspection and to provide topical anesthesia to the central tracheobronchial tree using 1-2% lidocaine as per routine clinical practice.

3. *Robotic assisted bronchoscopy*: Following airway inspection and application of topical anesthesia, the conventional thin bronchoscope will be removed and the Monarch platform (Auris Health, Inc, Redwood City, CA) will be connected to the endotracheal tube. Navigation to the peripheral pulmonary lesion will be performed by advancing the outer sheath and inner scope of the robotic bronchoscope to the targeted bronchus using a control pad. Once the outer sheath has been positioned appropriately, the inner scope will be advanced into the lung periphery towards the targeted lesion using the Monarch navigation (based on electromagnetic navigation and direct vision) as well as reference CT images for guidance.

4. *Radial probe endobronchial ultrasound:* the radial endobronchial ultrasound probe (R-EBUS) will be inserted into the working channel of the endoscope and advanced beyond the tip of the inner scope as the inner scope is advanced into the lung periphery towards the targeted lesion. As the endoscope is guided towards the targeted lesion, R-EBUS will confirm successful lesion localization prior to biopsies being performed. If lesion localization cannot be confirmed with R-EBUS, peripheral biopsies may still be performed using the Monarch platform. In these cases, if rapid on-site evaluation is "non-diagnostic", the robotic bronchoscope will be removed and the bronchoscopist may proceed to the salvage bronchoscopy procedure (as described below).

5. *Biopsy*: following lesion localization confirmation using R-EBUS, biopsy of the peripheral lesion will be performed using transbronchial needle aspiration (TBNA) and transbronchial biopsy (TBBx) as per standard clinical practice. Should TBNA be diagnostic using rapid on-site evaluation, no further biopsies are needed unless clinically indicated. Should rapid on-site evaluation be non-diagnostic from TBNA, a minimum of 3 TBNA and 3 TBBx will be performed, with the option to perform additional biopsies using additional instruments at the discretion of the clinician.

6. *Salvage procedures*: in cases in which R-EBUS cannot confirm the successful localization of peripheral lesions following use of the Monarch Endoscopy Platform navigation, the robotic bronchoscope will be removed and the bronchoscopist may proceed with peripheral bronchoscopy using flexible bronchoscopy and conventional guided bronchoscopic approaches which may include electromagnetic navigation, virtual bronchoscopic navigation and radial probe endobronchial ultrasound as per standard

medical care. R-EBUS will be used to confirm lesion localization prior to biopsy, which will be performed as outlined above in #4 and #5.

7. *ROSE:* ROSE will be performed in all cases. Tissue samples will be plated on slides for immediate on-site evaluation by the cytopathology team, as per the standard practice of the Investigational centers. ROSE of acquired cytologic specimen will be performed in all cases.

8. *Following bronchoscopy*: patients will be recovered in post-procedure recovery room as per standard institutional practice. A chest x-ray will be performed within 2 hours to assess for pneumothorax. Prior to hospital discharge, the investigator and/or designee will make sure that there are no SAE.

Duration of subject participation

Once the subject has completed 24 hours follow-up (24-84 hours window) without study related adverse events requiring further follow-up, subject will be exited from the study. For the study procedure conducted on Friday, the 24-hours follow-up visit (phone call) is acceptable to be conducted on the following Monday.

Assessment schedule

The following page outlines the required study assessments.

Table 1. Schedule of Assessments

Test/Parameter	Screening/ Baseline	Pre-Procedure	Procedure	Discharge	24-84 hr phone call	Study exit
Informed Consent	X					
Pregnancy Test (if applicable)	X					
Preliminary Qualification (inclusion/exclusion criteria)	X					
Medical History (pulmonary status)	X					
Physical examination		X				
Blood test and coagulation test (PT/INR)[1]	X					
HRCTScan[2]	X					
Fluoroscopy[3]			X			
Radial probe Endobronchial ultrasound (R-EBUS) [4]			X[4]			
Rapid on Site Evaluation (ROSE)			X			
Chest X-ray[5]				X[5]		
Concomitant medications[6]	X	X				
Follow-up Form				X	X	X
Navigation/control evaluation			X			
Biopsy sample evaluation			X			

[1] A blood test including the PT/INR coagulation test will be assessed before the procedure as per standard institutional practices.
[2] The procedure will take place within 14 days of CT scan for participation in the study.
[3] Fluoroscopy will be used in conjunction to provide an additional viewing method during the procedure.
[4] R-EBUS will be used to confirm the presence of a lesion.
[5] Chest X-ray within 2 hours from the conclusion of the procedure.

[6] Aspirin, clopidogrel and oral anticoagulants will be stopped as per routine clinical practice and coagulations tests will be performed before procedure. Anticoagulants will be restarted 24 hours after procedure if no bleeding persists. Subcutaneous anticoagulants will be stopped 24 hours before and restarted 24 hours after procedure if no bleeding persists.

Informed Consent. A study specific, IRB approved written informed consent must be obtained for all patients who are potential study candidates before any study-specific tests or procedures are performed.

Pregnancy Test (if applicable). If there is the potential for pregnancy, a pregnancy will be assessed with self-reporting before entry into the study.

Preliminary qualification (Inclusion/Exclusion criteria). Principal Investigator is responsible for certifying that key personnel have received adequate training to ensure they are aware of the regulations governing human subjects research and understand and adhere to the IRB-approved research protocol. Compliance with these standards provides assurance that the rights, safety, and well-being of human subjects are protected and the integrity of the data collected. Potential study candidates must meet the study specific Inclusion/Exclusion criteria based on the screening assessment. For the purpose of this study, a peripheral lung lesion is defined as a lesion located in a sub segmental branch of the bronchial tree that cannot be accessed by convex probe endobronchial ultrasound.

Medical history. During the screening/baseline assessment, the investigator or coordinator will record details of medical history as they relate to pulmonary status.

Physical examination. The investigator will perform a brief, directed physical and pulmonary examination and document any preoperative abnormalities.

Blood tests including the PT/INR coagulation test. These tests may be needed before the procedure to ensure that study patients have no problems related to blood clotting. (see above). Bleeding can sometimes occur after bronchoscopy, especially if tissue samples are taken. The study patients will be asked to stop anticoagulants several days prior to the procedure (see Table 1. above).

HRCT scan. CT analysis will require a full inspiratory CT scan. CT Scans should be performed no longer than 14 days pre-procedure as part of screening assessment. Specific CT parameters for scanner model and manufacturer will be provided to the site.

Fluoroscopy. Fluoroscopy will be used in conjunction with the bronchoscopy to provide an additional viewing method during the procedure.

Radial probe endobronchial ultrasound (R-EBUS). R-EBUS will be used to confirm the presence of a lesion.

Chest X-ray. Patients will undergo a routine chest X-ray within 2 hours from the conclusion of the procedure to o rule out complications such as pneumothorax.

Concomitant Medications. Principal investigator will determine relevant disease/procedure specific concomitant medications that is important for a study conduct.

Follow-up. The 24 hours (24-84 hours) follow-up will be a phone consultation.

Navigation/Control evaluation. The system navigation/control will be evaluated and recorded on the procedure CRFs.

Biopsy sample evaluation. Content and adequacy of biopsy samples will be assessed by pathologist or cytotechnologists using the rapid on-site evaluation (ROSE) in all cases. A preliminary diagnosis will be recorded. The final histopathologic diagnosis will be recorded on the 24-84 hours follow-up CRF.

Follow-up

The subject will have a follow-up phone call on day 1 post procedure (24-84 hours to accommodate procedure performed on Friday). Study coordinator or principal investigator will make 3 attempts within 24-84 hours follow-up window to reach the patients. The 24-84 hours CRF will be completed following the call.

Study Exit

Once the subject has completed 24-hours follow-up or has withdrawn, they should be exited from the Study provided they do not have any conditions that require continued follow-up. The date of exit and subject status will be recorded on the Study Completion Form. Data entry of the final biopsy diagnosis in non-diagnostic and indeterminate cases should be entered when available.

Criteria for Terminating Study

Auris Health, Inc reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of patients. Investigators and associated IRB will be notified in writing in the event of termination.

Possible reasons for study termination include:

- The discovery of an unexpected, significant, or unacceptable risk to the patients enrolled in the study.
- A decision on the part of Auris Health, Inc to suspend or discontinue development of the device.

Criteria for Suspending/Terminating a Study Center

Auris Health, Inc reserves the right to stop the study center at any time after the study initiation visit if no patients have been enrolled or if the center has multiple or severe protocol violations without justification or fails to follow remedial actions.

Possible reasons for suspending/terminating a study center include:

- Repeated failure to complete case report forms prior to scheduled monitoring visits.
- Failure to obtain written Informed Consent.
- Failure to report CEC Events/SAE/UADE to Auris Health, Inc. within 24 hours of knowledge.

4.3 Investigational product

The Auris Bronchoscope is the patient interfacing component of the Monarch Endoscopy Platform. Additional components of the platform are Auris Cart (AC) and the Auris Tower. The current platform received 510(k) clearance as a Class II device in March 2018. The system has several components that interface to the Auris Cart including: The Fluidics Control, Electro-Magnetic Field generator, and Reference Electro-Magnetic sensors.

Bronchoscope

The Auris Bronchoscope is a comprised of two collinear and concentric devices, the inner scope and the outer sheath both of which possess 4-way steering control. This configuration enables the capability of telescoping, which enhances the bronchoscope stability and access capability.

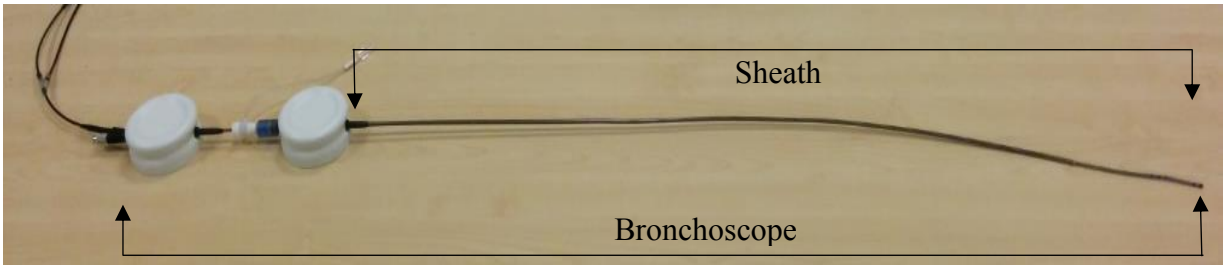


Figure 2. Auris Bronchoscope

The bronchoscope includes a camera that provides the operative perspective, an integrated light source in the scope handle and a 2.1 mm inner diameter working channel for the passing of tools.

The scope and sheath has a distal section capable of achieving articulation in pitch, yaw and any combination of the two to enable precise control while driving the bronchoscope. Proximally, the scope is equipped with a valve to facilitate the insertion and sealing of various ancillary devices, such as a biopsy needle. Additionally, the proximal section routes irrigation and aspiration to the shared working channel.

Auris Cart

The Auris Cart (AC) is a carrier for the robot arms. It includes two arms which contain rotary pulleys to actuate the drive cables in the bronchoscope. The Cart houses the electronic systems required to power and operate the Auris system. Automated lift controls will raise and lower the height of the robotic arms. The cart handle allows the cart to be maneuvered so that the cart wheels can be directionally locked. An embedded touch-screen on the cart handle provides feedback during system setup.

An Emergency Stop button (Estop) sits on the Auris Cart and is positioned such that a clinical assistant has easy access to it.

The following image shows the Auris Cart with the arms in the stow position (left) and load bronchoscope position (right):

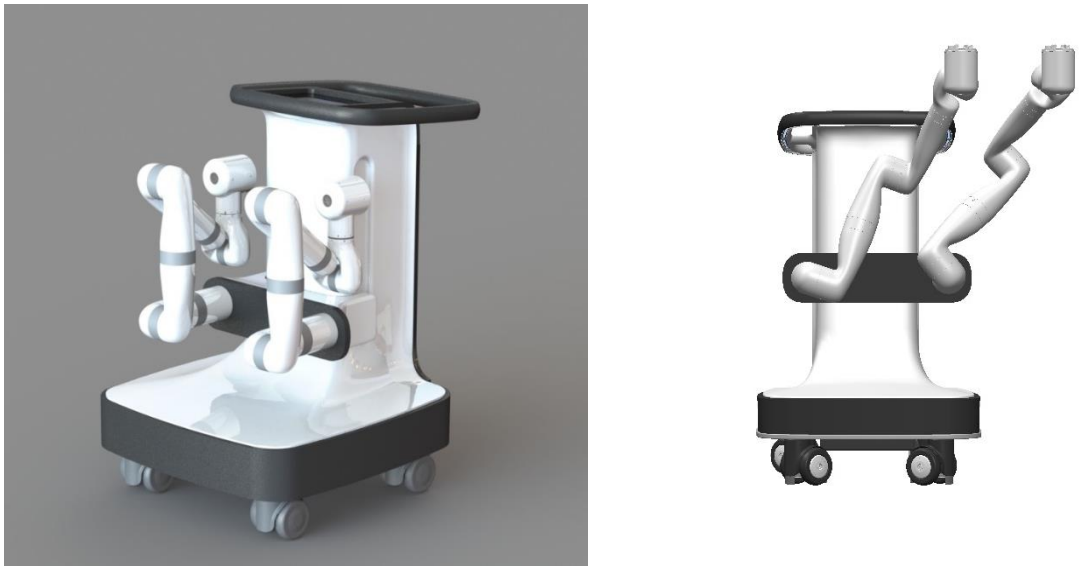


Figure 3. Auris Cart

Auris Tower

The Auris Tower houses two computers that run the system, a Non-Real Time Computer and a Real-Time Computer. The Non-Real-Time computer takes the inputs from the pendant, keyboard, mouse, camera, EM Localization/Targeting System and Power Distribution Unit.

The Non-Real-Time computer also contains an interface to the micro camera at the tip of the Endoscope. The camera interface performs the necessary image processing and generates output video streams.

The robotic system algorithms are also implemented on the Real-Time computer. The Real-Time computer receives inputs from the Non-Real-Time computer. The network handles communication between the two computers, robotic arms and Power Distribution Unit.

The tower provides connectivity for the bronchoscope camera and lighting, as well as the fluidics system.

A single monitor is integrated into the Tower to display real time video captured from the bronchoscope camera overlaid with information on the status of the robotic system. Lastly, an E-stop sits on the Auris Tower and is positioned such that a clinician has easy access to it. The following image show the Tower:

Figure 4. Auris Tower

The Tower includes an endoscopy controller that allows the clinician to control the system during a procedure. On the controller, two joysticks are used to drive and articulate the bronchoscope while various buttons are used to control irrigation, aspiration and the device state. The following image shows the endoscopic controller:

Figure 5. Auris Endoscopy Controller

Auris Cart External Components

The system has several components that interface to the Auris Cart including: Fluidics Control, Electro-Magnetic Field generator, and Reference Electro-Magnetic sensors.

Fluidics Control

The fluidics control consists of a peristaltic pump and controlled valves. The fluidics control can dispense a fluid through a single-use tubing set into the endoscope. The fluidics control actuates aspiration of fluids to an external vacuum source.

Electro-Magnetic Field generator

The Electro-Magnetic Field generator is used as part of the system for navigation guidance.

Reference Electro-Magnetic sensors

The Reference Electro-Magnetic sensors are used to monitor the patient position relative to the Electro-Magnetic Field Generator.

Device Labeling

A copy of the Instructions for Use (IFU) will be included with the devices.

Device Distribution

The Monarch platform will be provided free of charge to the investigator for his exclusive use in this study for 45 calendar days. The first day will be considered the first Monday following the completion of the required PI and staff training. The robotic bronchoscopes and other disposables required to perform the robotic bronchoscopy procedure with the Monarch Endoscopy Platform will be provided free of charge. Unused bronchoscope and disposables will be returned to Auris.

Device Accountability

Auris Health and Investigative Sites will maintain device accountability as required for this Study.

Return of Materials Upon Study Termination

Unless other arrangements have been made, the Monarch platform will be returned to Auris at the end of the 45 days enrollment. All used bronchoscopes may be returned to Auris for examination after every case.

5. Criteria for subject withdrawal

While study withdrawal is discouraged, patients may withdraw from the study at any time, with or without reason and without prejudice to further treatment. In all cases of

withdrawal, the reason(s) for withdrawal (if given) will be recorded upon study termination.

In addition, the investigator may withdraw the subject due to any of the following situations:

- adverse event
- any other reason determined by the investigator to be in the best interest of the subject.

Subjects withdrawn from the Study prior to insertion of the ABS should be converted to conventional bronchoscopy. Subjects withdrawn due to an adverse event should be followed until the event has been resolved or is stable, if at all possible.

5.1 Subject inclusion criteria

Pre-Procedure Inclusion Criteria	1. 18 to 80 years of age; 2. Capable and willing to give informed consent; 3. Acceptable candidate for an elective, non-emergent bronchoscopic procedure; 4. Solid peripheral lung lesions suspected of malignancy, between 1-5cm in size identified on thin slice CT scan within 14 days of the intended bronchoscopy 5. Lack bleeding disorders

5.2 Subject exclusion criteria

Pre-Procedure Exclusion Criteria	Subjects will be excluded from participating in this Study if they meet any of the following criteria prior to initiation of the endoscopic procedure: 1. Medical contraindication to bronchoscopy; 2. Patients with a subsolid nodule and/or ground-glass opacity lesions on pre-procedure chest CT 3. Patients with endobronchial involvement seen on chest CT 4. Lack fitness to undergo flexible bronchoscopy as determined by the bronchoscopist prior to procedure, and 5. Participation in any other investigational clinical trial (device or medication) 30 days before and throughout the duration of the study; 6. Uncontrolled or irreversible coagulopathy; 7. Female subjects who are pregnant or nursing or those of child-bearing potential refusing a pregnancy test; 8. Have significant mediastinal lymphadenopathy on chest CT scan and/or PET CT abnormalities suggestive of advanced stage lung cancer with mediastinal lymph node involvement

In addition, subjects will be excluded from participating in this Study if any of the following exclusion criteria occur during the endoscopic procedure:

Intra-Procedure Exclusion Criteria	Any presenting condition discovered intra-procedurally that in the opinion of the investigator would make participating in this study not in the patient's best interest.

6. Treatment of subjects

This study is not associated with any treatment. The bronchoscopy procedure to obtain a biopsy sample for diagnostic purposes is previously described in this protocol.

7. Assessment of efficacy

Primary Effectiveness Endpoint

The primary effectiveness endpoint is the successful navigation to targeted peripheral pulmonary lesions sized 1-5cm as confirmed using radial probe endobronchial ultrasound. Radial probe endobronchial ultrasound will be used in all cases to confirm the presence of a lesion immediately before performing biopsy.

Secondary Effectiveness Endpoint

The following will be considered secondary endpoints:

- Time to R-EBUS confirmation (lesion localization)
- Time to the tissue acquisition confirmation
- Total procedure time (from introduction to removal of the bronchoscope) and procedure interruptions
- Radiographic and procedural factors that influence the ability to successfully navigate to peripheral lesions including size and location of peripheral lesions
- Diagnostic yield
- Conversion to conventional bronchoscopic procedure (salvage procedure)

Time to R-EBUS confirmation: Is defined by the time the ABS bronchoscope is inserted into the oropharynx until the localization of the targeted lesion is confirmed by REBUS.

Time to the tissue acquisition confirmation: Is defined by the time the ABS bronchoscope is inserted into the oropharynx until the tissue acquisition is confirmed by the ROSE.

Total procedure time: Total procedure time is defined by the time the ABS bronchoscope is inserted into the oropharynx until the time a biopsy tool is removed.

Procedure interruptions: The sum of procedure interruptions due to platform malfunctions

Radiographic and procedural factors that influence the ability to successfully navigate to peripheral lesions including size and location of peripheral lesions: the following factors will be considered:

- Lesion size (recorded as the longest axis diameter)
- Lesion Location
- Presence or absence of a visible bronchus
- Procedure duration (measured from time of scope insertion)
- Type and amount of sedation provided
- Ability to localize peripheral lesions as confirmed by R-EBUS
- R-EBUS image characterization (concentric vs eccentric)
- Proximity of RES scope to peripheral lesion at the time of biopsy
- Distance of lesion from main carina as measured by electromagnetic navigation
- Bronchus generation count accessed by the Monarch
- Need to convert to salvage procedures
- Procedural time from scope in to scope out and total time if salvage procedure performed.
- Distance from scope to the targeted nodule as measured by navigation

Diagnostic yield will be determined from the results of the bronchoscopy. A biopsy that results in a specific diagnosis, either malignant or benign, will be assumed to be a true positive. Follow up of non-diagnostic or indeterminate biopsy results will be performed as clinically indicated. The diagnosis of "inflammation" will be considered diagnostic if follow up imaging results in improvement or resolution of the targeted lesion. In cases where the lesion is unchanged or has increased in size, the description of "inflammation" will be considered non-diagnostic.

Conversion to conventional bronchoscopic procedure:

Number of the procedure converted to the conventional bronchoscopy for any reason.

8. Assessment of safety

Primary Safety Endpoint

Number of device related adverse events.

Secondary Safety Endpoint

Number of complications unrelated to device.

Adverse Events

All adverse events (AE) and serious adverse events (SAE) will be monitored from the time of enrollment through the study exit.

An AE is defined as any undesirable clinical occurrence in a patient whether or not it is considered to be device related. In addition, the definition of AE applies to any event with an onset post study procedure or to any underlying diseases, present at baseline, that exacerbate in severity post study procedure. Therefore, an underlying disease that was present at the time of enrollment is not reported as an AE, but any increase in the severity of the underlying disease is to be reported as an AE. All reported AEs must be recorded in the database. A description of the event, including the start date, resolution date, action taken, and the outcome should be provided, along with the Investigator's assessment of the relationship between the AE, the study treatment and the study procedure.

The following definitions for rating severity of adverse events will be used:

Mild:	Awareness of signs or symptoms, but easily tolerated; are of minor irritant type; causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs or symptoms are transient.
Moderate:	Interferes with the subject's usual activity and/or requires symptomatic treatment.
Severe:	Symptom(s) causing severe discomfort and significant impact of the subject's usual activity and requires treatment.

A serious adverse event (SAE) is defined as an event which leads to:

- Death due to any cause
- Life-threatening condition
- Results in persistent or significant disability/incapacity
- Requires in-patient hospitalization or prolonged hospitalization
- Necessitates an intervention to prevent a permanent impairment of a body function or permanent damage to a body structure
- Results in congenital abnormality

All SAE's will be reported.

Device-Related Adverse Event*:* an adverse event is considered to be device-related when, in the judgment of the Investigator, the clinical event has a reasonable time sequence associated with use of the **MONARCH PLATFORM** and is unlikely to be attributed to concurrent disease or other procedures or medications. It is reasonable to believe that the system directly caused or contributed to the adverse event.

Procedure-Related Adverse Event*:* an adverse event is considered to be procedure-related when, in the judgment of the Investigator; it is reasonable to believe that the event is associated with the assigned study procedure and is not specific to the **MONARCH PLATFORM**

used. Other products, surgical techniques, or medications required specifically for the procedure are likely to have contributed to the occurrence of the event.

Concomitant Medication-Related Adverse Event: an adverse event is considered to be concomitant medication related when, in the judgment of the Investigator, it is reasonable to believe that the event is associated with concomitant medications used in conjunction with the **MONARCH PLATFORM AND** is not otherwise specific to the **MONARCH PLATFORM** (e.g. bleeding associated with anticoagulation medication).

Pre-Existing Condition-Related Adverse Event: an adverse event is considered to be related to a pre-existing condition when, in the judgment of the Investigator, it is reasonable to believe that the event is associated with the subject's pre-existing condition and is not specific to the **MONARCH PLATFORM** or procedure. Pre-existing conditions that are aggravated or become more severe during or after the procedure should be evaluated on a case-by-case basis to determine if the event may be more appropriately classified as device-related or procedure-related.

Site PIs will be responsible for identifying adverse events during the procedure and during the standard of care follow-up period. Site PIs will review adverse events experienced by subjects treated at their site during the procedure standard of care follow-up period and will record them in the medical record. Site PIs will review all adverse events, expected or unexpected, per standard medical care.

Site PIs will classify AEs as expected or unexpected, and report AEs directly to the sponsor and IRB per local IRB reporting policy. The lead investigator will capture all AEs occurring at all sites, including unanticipated AEs, in the electronic data capture instrument. Auris Health, Inc., or its designee, may assist the Investigator in determining potential reportability to the FDA and other regulatory authorities as an Unanticipated Adverse Device Effect (UADE).

The Investigator should follow all unresolved serious adverse events until the events are resolved, the subject is lost to follow-up, the subject has withdrawn consent, or the adverse event is otherwise explained.

For purposes of this study, the following events are not likely to be device-specific adverse events, because they are typical procedure/anesthesia related adverse events normally expected to occur in conjunction with these types of bronchoscopic procedures / post-procedure, or are associated with customary, standard care of subjects undergoing these procedures:

- Any pre-planned surgical procedures
- Bleeding
- Pneumothorax
- Post-procedure respiratory insufficiency

This listing of events is intended to provide guidance to the investigational sites for purposes of adverse event reporting. The Investigator at the investigational site should utilize his/her own clinical judgment in evaluating adverse experiences, and may decide that the above events should be reported as adverse events.

General Reporting Requirements (Serious & Non-Serious Adverse Events)

All serious and potentially device- and/or procedure-related adverse events must be recorded on the Adverse Event CRF by the Investigator (or designee). The report should include: severity, duration, action taken, treatment outcome and relationship of the adverse experience to the study device, procedure, concomitant medications, pre-existing condition, etc. (i.e., unrelated, related or relationship unknown).

In the case of serious adverse events, procedure and/or device observations and malfunctions, medical record documentation (e.g. procedure notes, operative notes, discharge summary, relevant progress notes, imaging or lab studies) must be provided to Auris or its designee.

The following criteria must also be adhered to by the Investigator in the case of serious adverse events:

- The Adverse Event CRF must be signed by the Investigator or Co-Investigator.
- It is the responsibility of the Investigator to inform their EC of serious adverse events as required by their EC procedures and in conformance with FDA and local regulatory requirements.

All serious adverse events must be reported by the Investigator (or designee) to the sponsor, within 24 hours of learning of the adverse event via CRF. The Auris contact information for questions is:

Auris Health, Inc

150 Shoreline Dr
Redwood City, CA 94065

Attn: Emir Deljkich

Email: emir.deljkich@aurisrobotics.com

Phone: (650) 743-4346

Device Failures and Malfunctions

All reported device observations, malfunctions or failures of the MONARCH ENDOSCOPY PLATFORM are required to be documented in the CRF. Device failures and malfunctions should also be documented in the patient's medical record.

NOTE: Device failures or malfunctions are NOT to be reported as adverse events. However, if there is an adverse event that results from a device failure or malfunction, that specific event would be recorded in the usual way.

9. Statistical Methods

Descriptive statistics will be calculated to characterize study subjects and endoscopic procedures, and will include the mean±SD for continuous variables and percentages for categorical variables, such as subject's age, location of peripheral lesions, ultrasound

characteristics, duration of procedure, type and amount of sedation administered, and adverse events.

10. Access to source documentation

The Principal Investigator must maintain detailed source documents on all Study subjects who are enrolled in the Study or who undergo screening. Additionally, the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB review and regulatory inspection(s) by providing direct access to source data and documents. Potential source documents include subject medical records including: hospital charts, clinic charts, Investigator's subject Study files, as well as the results of diagnostic tests (e.g., laboratory tests).

The following minimum information should be recorded in the subject's medical records:

- The date the subject entered the Study and the subject number
- The Study protocol number and the name of the Sponsor
- The date that informed consent was obtained
- Evidence that the subject meets Study eligibility requirements (e.g., medical history, Study procedures and/or evaluations)
- The dates of all Study related subject visits
- Evidence that required procedures and/or evaluations were completed
- Use of any concurrent medications
- Documentation of specific device used, if any
- Occurrence and status of any Adverse Events
- The date the subject exited the Study, and a notation as to whether the subject completed the Study or was discontinued, including the reason for discontinuation.

Record Retention

The Investigator will maintain all essential Study documents and source documentation, in original format, that support the data collected on the study patients in compliance with the ICH/GCP guidelines. Documents must be retained for at least 2 years after the last approval of marketing application or until at least 2 years have elapsed since the formal discontinuation of the clinical investigation of the product. These documents will be retained for a longer period of time by agreement with Auris Health, Inc or in compliance with other regulatory requirements. When these documents no longer need to be maintained, it is Auris's responsibility to inform the Investigator. The Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the Investigator withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility. Auris Health, Inc must receive written notification of this custodial change.

11. Quality control and quality assurance

Site Training

To ensure accurate, complete, and reliable data, the Sponsor or its representatives will provide instructional material to the Study sites, as appropriate;

- Instruct the Investigators and Study personnel on the protocol, the completion of the CRFs, and Study procedures
- Communicate regularly with site personnel via mail, email, telephone, and/or fax
- Make periodic visits to the Study sites.

During those visits, the sponsor's designee will monitor the subject data recorded in the CRFs against source documents at the Study site.

Physician Training

Prior to enrolling subjects in the Study, investigators will be provided didactic training on the procedural steps required to use the Monarch platform. Physicians who have not previously used the device will receive training with a Sponsor-designated proctor using a benchtop model to simulate the use of the Monarch platform.

Audits and Inspections

The Principal Investigator for the site will inform the Sponsor or the Sponsor's designee in advance if they are to be audited or inspected by any regulatory agencies. The Sponsor or the Sponsor's designee will also inform the site if they are made aware of a pending audit or inspection by a regulatory agency. No FDA inspections are expected to be associated with this Study.

Amending the Protocol

An Investigator may not make protocol changes without prior approval by Auris Health. All significant protocol changes that may affect the following must be submitted and approved by the IRB before initiating the change:

- validity of the data or information resulting from the completion of the approved protocol;
- relationship of the likely subject risk to benefit relied upon to approve the protocol;
- scientific soundness of the investigational plan, or;
- rights, safety, or welfare of the human subjects involved in the investigation.

Auris will submit a copy of the protocol amendment to the Investigator for his IRB to review. The investigative site must send Auris Health a copy of the IRB approval letter for the protocol amendment.

Auris may make certain administrative changes to the protocol without prior approval of the IRB. The site IRB will be notified of these changes.

Emergency Actions

Auris Health, Inc accepts the right of the Investigator to deviate from the protocol in an emergency when necessary to safeguard the life or the physical well-being of a study patient. The Investigator must give notice of any emergency deviations and justification for the deviation to Auris Health, Inc and the IRB as quickly as possible after the episode, in any event no later than 24 hours after the emergency.

Protocol Deviations

A protocol deviation is defined as an event where the Clinical Investigator or site personnel did not conduct the study according to the protocol.

Investigators shall be required to obtain prior approval from Auris management before initiating deviations from the protocol, except where necessary to protect the life or physical well-being of a subject in an emergency. Such approval shall be documented in writing and maintained in clinical study management and Investigator files. Prior approval is generally not expected in situations where unforeseen circumstances are beyond the Investigator's control, (e.g. subject was not available for scheduled follow-up office visit, blood sample lost by laboratory, etc.); however, the event is still considered a deviation and will be reported via the appropriate CRF.

Deviations must be reported to Auris Health regardless of whether medically justifiable, pre-approved by Auris Health or taken to protect the subject in an emergency. Subject specific deviations will be reported on the Protocol Deviation case report form. Non-subject specific deviations, (e.g. unauthorized use of the **STUDY DEVICES** outside the study, unauthorized use of the **STUDY DEVICES** by a physician who has not signed an Investigator agreement or not been trained in the use of the devices, etc.), will be reported to Auris Health via the appropriate CRF. Investigators will also adhere to procedures for reporting study deviations to their IRB in accordance with their specific IRB reporting policies and procedures.

Regulations require that Investigators maintain accurate, complete and current records, including documents showing the dates of and reasons for each deviation from the protocol. For reporting purposes, Auris classifies study deviations as major and minor:

*Major deviation***:** Any deviation from subject inclusion and exclusion criteria, subject informed consent procedures or unauthorized device use.

*Minor deviation***:** Deviation from a protocol requirement such as incomplete/inadequate subject testing procedures, follow-ups performed outside specified time windows, etc. Minor Deviations that continue to occur at an investigational site may be classified as Major Deviations if corrective action is not taken to secure future compliance to the protocol.

Coverage of Expenses

The treated subjects will not be reimbursed or compensated for participating in the Study.

Confidentiality

Confidentiality of subjects will be maintained throughout the Study. A unique identification code will be assigned to each subject participating in this Study. Any data that may be published in abstracts, scientific journals, or presented at medical meetings will reference a unique subject code and will not reveal the subject's identity. The Sponsor will make every reasonable effort to protect the confidentiality of the subjects participating in the Study.

12. Ethics

Study Conduct & the Declaration of Helsinki

The Study will be performed in accordance with the relevant parts of Title 21 CFR Parts 812, 50, 54, 56 and ISO 14155-1 / 14155-2.1; the ICH Guidelines for Good Clinical Practices (E6), the Declaration of Helsinki, and any regional and/or national regulations.

Institutional Review Board/Ethics Committee

A copy of the protocol, proposed Informed Consent form, other written patient information and any proposed advertising material must be submitted to the EC for written approval. A copy of the written EC approval of the protocol and Informed Consent form must be received by Auris Health, Inc. before recruitment of patients into the study.

The Investigator must submit and, where necessary, obtain approval from the IRB for all subsequent significant protocol amendments and significant changes to the Informed Consent form. The Investigator should notify the IRB of deviations from the protocol or SAEs and UADEs occurring at the site and other SAE/UADE reports received from Auris Health in accordance with local procedures.

The Investigator will be responsible for obtaining annual IRB approval and renewal throughout the duration of the study. Copies of the Investigator's reports and the IRB continuance of approval must be sent to Auris Health.

Informed Consent Form

Written Informed Consent must be obtained for all patients who are potential study candidates before any study-specific tests or procedures are performed.

Patients who meet general entry criteria will be asked to sign the study-specific, IRB approved Informed Consent form before any study-specific tests or procedures are performed. Study personnel should explain that even if a patient agrees to participate in the study and signs an informed consent form, the screening observations may demonstrate that the patient is not a suitable candidate for the study.

Informed consent will take place in a private environment (e.g. patient exam room), free from distractions. The PI will approach the subject at their standard of care clinic appointment or prior to their scheduled study procedures and will explain the study to qualified subjects prior to obtaining consent. Interviews to obtain consent will not follow

any stressful situation (e.g. patient being informed he/she may have cancer) and will not be conducted if the patient has received any mind-altering medications or anesthesia. Patients will be assessed for their capacity to consent by the ability to show comprehension of the procedure, ask appropriate questions, and appear properly oriented. A signed copy of all consents and the HIPAA authorization document will also be given to consenting subjects.

A Screening/Enrollment Log will be maintained to document select information about candidates who fail to meet the entry criteria.

A sample Informed Consent form is provided in Section 21 Attachment 2 for the Investigator to prepare for use at his/her site. The written Informed Consent documents should be prepared in the language(s) of the potential patient population.

The reviewing IRB and the sponsor must first approve the Informed Consent forms that are used. The Informed Consent forms that are used should be in accordance with the current guidelines as outlined by the Good Clinical Practices (GCP) guidelines, Declaration of Helsinki and the International Conference on Harmonization (ICH).

Prior to participation in the clinical Study, each patient must give written Informed Consent after the context of the study has been fully explained to the patient in language that is easily understood by the patient. The patients must also be given the opportunity to ask questions and have those questions answered to their satisfaction.

Written Informed Consent must be recorded appropriately by means of the patient's, or their legal representative's dated signature. The patient will receive a copy of the Informed Consent form.

Investigator Responsibilities

- Agree to sign and adhere to the Investigator Agreement
- Agree to participate in Investigator meetings as scheduled by Auris Health, Inc
- Be willing to provide required assessments for analysis
- Be willing to perform and be capable of performing treatment procedures as outlined in this protocol
- Comply with all required elements of this protocol (e.g., perform testing and follow-up as specified, especially during personnel transitions) and supply material suitable for quantitative analysis
- Agree to obtain written Informed Consent before any study specific procedures are performed in accordance with GCP
- Complete all CRFs prior to scheduled monitoring visits

13. Data Handling and recordkeeping

Standardized electronic CRFs will be utilized by participating site using a standardized database. Electronic data capture system will be used in this study. Investigator is

responsible for the accurate completion and timely submission of the data collected during the Study. Incoming data will be monitored by the sponsor or designee to identify inconsistent or missing data and any adverse events. Any data issues are to be promptly addressed with the investigator. Quality assurance procedures will be established to ensure that complete, accurate and timely data are submitted, that protocol requirements are followed and that complications, adverse events and adverse device effects are correctly reported and investigated, as appropriate. Investigator is to maintain all source documents as required by the protocol, including laboratory results, supporting medical records, and signed Informed Consent forms. The source documents will be used during the regular monitoring visits to verify information from the database against data contained on the completed CRFs.

The Principal Investigator must maintain detailed records on all subjects who sign the Informed Consent and begin the pre-procedure evaluation. Data for enrolled subjects will be entered into CRFs provided by the Sponsor. All data should be entered completely, promptly and legibly. For source documents, corrections should be made in a manner that does not obscure or eliminate the original error, by striking through the original data with one line, and initialing and dating the change, along with the reason for the change (if not obvious).

Study Exit CRFs are completed for all enrolled subjects, regardless if they did or did not complete the Study (e.g., subject discontinuation, Study termination). Data entry of the final biopsy diagnosis in non-diagnostic and indeterminate cases should be entered when available.

The PI will review the results, and the results will become part of the subject's medical record and research record. Any clinical follow-up or repeat procedures will be dictated by the patient's physician based on clinically relevant data and will not be influenced by enrollment into this study. All patient information will be de-identified through use of the 6-digit patient codes. All information and data related to this study will be stored in a secured, locked cabinet in a secure office accessible only by the PI.

Prior to each site initiation, the site PI and staff will participate in an educational teleconference with the Coordinating Site PI to ensure that all personnel fully understand the protocol, data collection instrument, and any other study related issues or documents. Contact information, including the phone and pager numbers for the principal investigators and study staff will be provided to all sites

In minimum, data on the following will be collected at all sites: radiographic characteristics, procedural characteristics, diagnostic yield, and complications:

1. *Radiographic information*: the radiographic information collected will include the following:

a) Lesion size (recorded as the longest axis diameter)

b) Location

c) Presence or absence of a visible bronchus

2. *Procedural characteristics*: procedural information will include the following:

a) Room preparation time

b) Robot set-up time

c) Procedure duration (measured from time of scope insertion)

d) Type and amount of sedation provided

e) Ability to localize peripheral lesions as confirmed by R-EBUS

f) R-EBUS image characterization (concentric vs eccentric)

g) Proximity of RES scope to peripheral lesion at the time of biopsy

h) Distance of lesion from main carina as measured by electromagnetic guidewire

i) Need to convert to salvage procedures

j) Procedural time from scope in to scope out and total time if salvage procedure performed.

3. *Diagnostic yield:* diagnostic yield will be determined from the results of the bronchoscopy. A biopsy that results in a specific diagnosis, either malignant or benign, will be assumed to be a true positive. Follow up of non-diagnostic or indeterminate biopsy results will be performed as clinically indicated and data entry of the final biopsy diagnosis in non-diagnostic and indeterminate cases should be entered when available. The diagnosis of "inflammation" will be considered diagnostic if follow up imaging results in improvement or resolution of the targeted lesion. In cases where the lesion is unchanged or has increased in size, the description of "inflammation" will be considered non-diagnostic.

4. *Complications*: the following complications will be recorded:

a) Pneumothorax as indicated by post-procedure chest radiograph

   a. Need for tube thoracostomy

b) Bleeding with severity determined by the need for intervention such as blood transfusion, inpatient hospitalization or escalation in level of care

Data Safety Monitoring Plan

All subjects enrolled in the trial will undergo routine standard of care bronchoscopy that is indicated as medically necessary by their physicians. Prior to the bronchoscopic procedure, PIs will explain the risks associated with bronchoscopy, and verify that the research only risks have been explained, and that the subject has signed an informed consent form. There are no anticipated risks, outside of the risk for the standard of care procedures for this clinical trial. All subjects are required to read, understand, and sign the informed consent form associated with the research study. Each subject will be

informed of post procedure symptoms of which to be aware that may represent adverse reactions to the bronchoscopy. Symptoms that the patient will be informed to look out for include:

- Pain or difficulty with swallowing
- Difficulty breathing
- Vomiting
- Dizziness
- Abdominal or chest pain
- Continuous bright red blood in your sputum
- Fever above 100.0 degrees Fahrenheit

If the subject notes any of these symptoms, he/she is instructed to contact his/her physician, who will determine the course of action. All events are to be reported within 48 hours of occurrence to the coordinating site (WUSM). All adverse events (AEs) will be reviewed by the medical monitor within one month of their occurrence and summarized for review. The PI at each site will be responsible for submitting this report to the IRB at his/her institution as required. AEs and other reportable events are defined below.

14. Monitoring

Monitoring visits to the clinical sites will be made periodically during the study by the Sponsor's designee to ensure that all aspects of the current, approved protocol/amendment(s) are followed. Original source documents will be reviewed for verification of data in the database. The Investigator/institution guarantees direct access to original source documents by Auris Health, Inc. personnel, their designees, and appropriate regulatory authorities. In the event that the original medical records cannot be obtained for a patient that is seen by a non-study physician at a non-study institution, photocopies of the original source documents must be made available for review.

It is important that the Investigator and relevant study personnel are available during the monitoring visits and that sufficient time is devoted to the process.

Phone contacts and site visits will be conducted to ensure that the protocol is being followed and that any protocol deviations are properly documented. Clinical monitoring will include a verification that Informed Consent was properly obtained for all enrolled study participants, a review of clinical records for accuracy and completeness, resolution of missing or inconsistent results and a review of source documents. The clinical monitor will verify that the Case Report Forms (CRFs) are in agreement with the source documentation and other records. The investigator will make available to the clinical monitor for review all Informed Consent documents, source documentation, original laboratory data and other relevant records for all enrolled subjects at the site. It is important

that the investigator and other relevant site personnel are available for consultation with the clinical monitors during the monitoring visits and that sufficient time is devoted at the site to the monitoring process.

Additionally, telephone and/or e-mail contact will be conducted on a regular basis with the investigator and the site staff to ensure that the protocol is being followed and to address any issues that may occur during the course of the Study.

If a deficiency is noted during an on-site visit (or at any other time during the course of the Study), the clinical monitor is required to discuss the situation with the investigator and the Sponsor (if required) to secure compliance.

15. Compensation, Insurance and Indemnity

The financial agreement, insurance and indemnity between sponsor and investigators are provided in separate agreements.

16. Publication policy

The existence of this clinical Study is confidential, and it should not be discussed with persons outside of the Study. Additionally, the information in this document and regarding this Study contains trade secrets and commercially sensitive information that is confidential and may not be disclosed unless such disclosure is required by regional or national law or regulations. Subject to the foregoing, this information may be disclosed only to those persons involved in the Study who have a need to know, but all such persons must be instructed not to further disseminate this information to others. These restrictions of disclosure will apply equally to all future information provided that is indicated as confidential.

The data generated by this clinical Study are the property of the Sponsor, Auris Health, Inc. These data may be used by the Sponsor and Investigators now and in the future for presentation or publication at Sponsor's discretion or for submission to governmental regulatory agencies. The Principal Investigators may publish or present the Study results with prior consent of the Sponsor, but will not disclose confidential information. Prior to submission by a Principal Investigator for publication or presentation, the Sponsor will be provided with the opportunity to review the submission for confidential information and accuracy.

17. Appendices

17.1 Appendix I

References:

1. Aberle DR, Adams AM, Berg CD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. The New England journal of medicine 2011; 365:395-409
2. Chen AC, Loiselle A, Zhou L, Baty J, Misselhorn D. Localization of peripheral pulmonary lesions using a method of CT-anatomic correlation and radial probe endobronchial ultrasound. Ann Am Thorac Soc 2016, 13(9):1586-1592.
3. Silvestri GA, Vachani A, Whitney D, Elashoff M, Ferguson JS, et al. A bronchial genomic classifier for the diagnostic evaluation of lung cancer. N Engl J Med 2015, 16;373:243-251.
4. Ost DE, Ernst A, Lei X, Kovitz KL, Benzaquen S, et al. Diagnostic yield and complications of bronchoscopy for peripheral lung lesions. Results of the AQuIRE registry. Am J Respir Crit Care Med 2016, 193(1):68-77.
5. Veronesi, G. Roboic lobectomy and segmentectomy for lung cancer: results and operating technique. Journal of Thoracic Disease 2015;7:S122-130.
6. Chen AC, Gillespie C. Robotic endoscopic airway challenge: REACH assessment. Ann Thorac Surg 2018 (in press).

17.2 Appendix II

Regulatory Considerations

Auris Health, Inc. in cooperation with the Investigator will make necessary efforts to ensure that this study is conducted in compliance with GCPs and all applicable regulatory requirements.

Role of Auris Health

As the sponsor of this clinical study, Auris has the overall responsibility for the conduct of the study, including assurance that the study meets all applicable regulatory requirements of the Food and Drug Administration (FDA). In this study, Auris may have certain direct responsibilities and may delegate other responsibilities to Consultants or Clinical Research Organization (CRO). Together, both Auris and its Consultants and CRO will ensure adherence to the sponsor's general duties. These regulations may include applicable portions of: (21 CFR 812.40), selection of Investigators (21 CFR 812.43), monitoring (21 CFR 812.46), supplemental applications (21 CFR 812.35 (a) and (b)), maintaining records (21 CFR 812.140 (b)), and submitting reports (21 CFR 812.150 (b)).

Sponsor may choose to appoint a steering committee for the study; this committee may include investigators, other experts not otherwise involved in the trial, and representatives of the sponsor. A sponsor may delegate and/or seek advice from trial steering committee members about study design, ongoing monitoring of study conduct and adjudication of individual adverse events. In addition, the trial steering committee members may be asked to participate in the analysis and/or interpretation of data as well as to revise manuscript(s) before submission.

Pre-Study Documentation Requirements

Prior to shipment of product, the following documents must be provided to Auris Health, Inc:

- Signed and dated Investigator Agreement
- A copy of the written EC approval of the protocol
- A copy of the written EC approval of the Informed Consent Form
- A copy of the curriculum vitae of the Principal Investigator and Co-Principal Investigator (if applicable)

General Duties [21 CFR 812. 40]

No IDE application to FDA is required for this Study. The Sponsor and the Investigator are responsible for obtaining IRB approval prior to start of the study. As the sponsor, Auris is also required to obtain signed study agreements, to provide the Investigators with the information necessary to conduct the study and adequate on-site training to conduct the

Study, to ensure proper clinical site monitoring, and to provide the required reports to the Investigators, and IRBs.

Auris will be responsible for providing quality data that satisfies publication requirements and informing of serious unanticipated adverse events and deviations from the protocol.

Monitoring [21 CFR 812. 46]

Sponsor will conduct investigational site monitoring to ensure that all Investigators are in compliance with the protocol and the Investigators' agreements. The sponsor and/or designee will monitor the sites to ensure that the completed Case Report Forms match the medical records, and resolve any differences. The sponsor will retain the right to remove either the Investigator or the investigational site from the study.

The sponsor will review significant new information, including unanticipated serious adverse events and ensure that such information is provided to the Investigators and to all reviewing IRB's.

Supplemental Applications [21 CFR 812. 335 (A) and (B)]

As appropriate, the sponsor will submit changes in the Investigational Plan to the Investigators to obtain EC re-approval. No FDA submissions are required.

Maintaining Records [21 CFR 812. 140 (B)]

The sponsor will maintain copies of correspondence, data, shipment of devices, serious adverse device effects and other records related to the clinical Study. The sponsor will maintain records related to the signed Investigator Agreements.

Submitting Reports [21 CFR 812. 150 (B)]

No FDA submissions are required for the Study.

Site Record Retention Policy [21 CFR 812. 140 (D)]

The sponsor and clinical sites will maintain all records pertaining to this study for a period of two years following: the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a pre-market approval application. Record retention dates will be provided to all concerned by the sponsor.

Informed Consent & Institutional Review Board/Ethic Committee [21 CFR Parts 50 & 56]

All subjects must provide written informed consent in accordance with the local clinical site's IRB. A copy of the consent form from each center must be forwarded to the Sponsor for review and approval prior to submitting it to the EC. The site must provide the Sponsor with a copy of the clinical site's EC approval letter and the informed consent. Yearly approvals for the continuation of the Study at each clinical site must also be forwarded to the Sponsor.

All Protected Health Information (PHI) to be collected in the study will be described in the informed consent form, and all study data will be managed in accordance with the Privacy Law (HIPAA).

17.3 Appendix III

Study Centers:

Institution	Location	Investigators
Washington University School of Medicine	660 S. Euclid Avenue St. Louis, MO 63110	PI: Alexander Chen, M.D., Lead Investigator Co-PI: N/A
Henry Ford Health System	2799 W Grand Blvd IM - Pulmonary K-17 Detroit, MI 48202	PI: Michael Simoff, M.D.
Cleveland Clinic	9500 Euclid Avenue Cleveland, OH 44195	PI: Thomas Gildea, M.D. Co-PI: Michael Machuzak, M.D. Co-PI: Joseph Cicenia, M.D.
Medical University of South Carolina	171 Ashley Avenue Charleston, SC 29425	PI: Gerard Silvestri, M.D. Co-PI: Nicholas Pastis, M.D.
Inova Fairfax Hospital	921 Telestar Ct Falls Church, VA 22042	PI: Amit Mahajan, M.D.

Coordinating Center:

Washington University School of Medicine
660 S. Euclid Avenue
St. Louis, MO 63110

Alexander Chen, MD

Note: Study centers not executing the Clinical Trial Agreement will not participate in the study.

17.4 Appendix IV

IRB Names:

IRB information will be kept separately.