Lungpacer®

AeroPace® System

User Guide

Rx Only

For use only with AeroPace System components.

650-0297, Rev E, 11-Mar-2025

Contents

Introduction

The AeroPace® System (a Temporary Transvenous Diaphragm Activation System) is intended for temporary stimulation of the phrenic nerve(s) to increase diaphragmatic strength in mechanically ventilated patients. The AeroPace System utilizes a temporarily placed, neurostimulation central venous catheter and an external bedside control unit, designed to operate in conjunction with mechanical ventilation in any mode, to transvenously stimulate the left and/or right phrenic nerves to strengthen the diaphragm and facilitate weaning. After placement of the AeroPace Neurostimulation Catheter, the AeroPace System is used to deliver 60 stimulations to contract the diaphragm twice a day, a total of 120 stimulations or diaphragm contractions daily, for up to 30 days. The sterile single-use AeroPace Neurostimulation Catheter also functions as a standard central venous catheter for use for up to 30 days.

Intended Use

The AeroPace System is intended for temporary stimulation of the phrenic nerve(s) to increase diaphragmatic strength.

The AeroPace System is intended for use in hospitals and hospital-type facilities which provide care for patients requiring mechanical ventilation. The device is intended to be used by appropriately trained personnel under the direction of a physician.

Indication for Use

The AeroPace System is indicated to improve weaning success – increase weaning, reduce ventilator days, and reduce reintubation - in patients ages 18 years or older on mechanical ventilation ≥ 96 hours and who have not weaned.

Trademarks

Lungpacer® Medical has the following trademarks associated with the AeroPace System. The name in parentheses is used throughout this User Guide to refer to the item.

- AeroPace® System (“System”)
- AeroPace® Neurostimulation Console (“Console”)
- AeroPace® Neurostimulation Console Cart (“Cart”)
- AeroPace® Neurostimulation Catheter Kit (“Catheter Kit”)
- AeroPace® Neurostimulation Catheter (“Catheter”)
- AeroPace® Catheter Cable (“Catheter Cable”)
- AeroPace® Airway Sensor (“Airway Sensor”)
- AeroPace® Airway Sensor Cable (“Airway Sensor Cable”)
- AeroPace® Handheld Controller (“Handheld Controller”)

Contraindications

Do not use the AeroPace System with active implanted cardiac pacemakers, defibrillators, or other implantable electronics within proximity to the AeroPace Neurostimulation Catheter. The AeroPace System has not been clinically evaluated for safety with these implantable electronic devices.

Warnings

WARNING: Read all AeroPace System warnings, cautions, and instructions prior to use. Failure to observe warnings for the AeroPace System may result in severe injury or death.

System Setup Warnings:

- Connect the Console power cord (the only means for mains disconnection) to an easily accessible “Hospital Only” or “Hospital Grade” AC mains outlet that is properly grounded with protective earth, and is compatible with the ratings printed on the Console label. Connecting the Console to an incompatible power source may result in fire or electrical shock.
- Do not modify the AeroPace System. Do not use or connect any devices to the AeroPace System or its components that are not described in this User Guide.
- The AeroPace System has not been evaluated for its interaction with all possible medical equipment under all operating conditions. Use of the AeroPace System outside of the Operating Conditions may result in injury. Do not use the AeroPace System with equipment likely to interact adversely with neurostimulation devices or central venous catheters. Assess all potential interactions before using the AeroPace System in conjunction with other medical equipment. The Use of accessories other than those specified may result in increased electromagnetic emissions or decreased electromagnetic immunity.

AeroPace Neurostimulation Catheter Insertion and Placement Warnings:

- Do not position the AeroPace Neurostimulation Catheter (or allow it to remain) in the right atrium, right ventricle, or in a position that may induce cardiac arrhythmia. Incorrect positioning of the Catheter may result in cardiac injury, arrhythmia, or cardiac tamponade.
- The AeroPace ECG feature is intended to function as an assistive aid in the placement of the AeroPace Neurostimulation Catheter. Do not use the AeroPace ECG feature to diagnose cardiac events or diseases.

Mapping and Therapy Warnings:

- Ventilator settings should be configured appropriately for the patient according to institutional guidelines. Observe the patient closely during System use to ensure that the ventilator settings and the AeroPace System settings are compatible. Failure to do so may result in inadequate ventilation, ventilator dyssynchrony, inappropriate Therapy delivery, or lung or diaphragm injury. See *“Therapy” on page 23* for details.
- Delivery of electrical stimulation in the right atrium, right ventricle, or other positions may result in cardiac arrhythmia. If unwanted patient effects (such as an arrhythmia) occur during Mapping or Therapy, stop stimulation immediately. If needed, perform Exclusion before restarting Mapping or Therapy. See *“Electrode Exclusion” on page 31* for details.

- The AeroPace Neurostimulation Catheter is MR Conditional, but the Neurostimulation Console is MR Unsafe. Conditions under which the AeroPace Neurostimulation Catheter is MR compatible and may be scanned safely are described in the Catheter Kit Instructions for Use. Always disconnect the Catheter from the Neurostimulation Console before conducting MRI, and keep the Console away from MR equipment.

Maintenance and Cleaning Warnings:

- To reduce the risk of electrical shock, disconnect mains power from the Console before cleaning.

EMC Warnings:

- Only accessories specified or provided by the manufacturer should be used with the AeroPace System. Use of accessories other than those specified may result in increased electromagnetic emissions or decreased electromagnetic immunity.
- Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the AeroPace System. Otherwise, degradation of the performance of the AeroPace System may occur, which may include the system safely entering a state where stimulation is not delivered.
- The AeroPace System should not be used while stacked or placed adjacent to other equipment, as this could result in improper operation of the AeroPace System or other equipment.

System Cautions

CAUTION:

- If external defibrillation or any medical treatment in which electrical current is passed through the patient's body from an external source is necessary, disconnect the AeroPace Neurostimulation Catheter from the Catheter Cable first. Failure to disconnect the Catheter before exposure to electrical current may result in non-effective defibrillation, and/or irreparable damage to the System. If a defibrillation event occurred with the Catheter connected to the Console, contact Lungpacer before subsequent use of the System.
- Do not expose the AeroPace Console, Catheter Cable, Sensor Cable, Handheld Controller, Sensor electrical connector or Catheter electrical connector to excessive moisture. In case of fluid ingress, disconnect the Catheter Cable from the Catheter, turn off the Console, unplug the power cord, dry the exterior of the components of the AeroPace System with a cloth, and wait for them to dry completely. Do not use the AeroPace System or any of its components if they appear compromised by fluid ingress. Fluid ingress into the System may cause device malfunction and may result in fire or electrical shock.
- Do not use the AeroPace System in an oxygen-rich environment such as a hyperbaric chamber. Doing so may result in fire.
- Do not use the Console if the enclosure is warm to the touch. Touching an overheated Console may cause injury.
- Do not expose the AeroPace System or any of its components to excessive heat. Overheated System or exposing System to fire may cause injury.

Potential Complications

The potential complications associated with central venous catheters are:

- Adverse tissue response
- Allergic reaction
- Arrhythmia
- Bleeding / Hemorrhage
- Bradycardia
- Bruising, swelling or seroma at insertion site
- Cardiac structure damage
- Central line-associated blood stream infection
- Cerebrovascular event
- Discomfort
- Embolism
- Hematoma
- Hemothorax
- Hypertension / hypotension
- Inadvertent arterial or venous puncture
- Infection
- Lung injury
- Lymphatic / thoracic duct injury
- Mediastinal injury
- Nerve injury
- Pain, tenderness, swelling, discomfort at access site
- Pneumohematoma
- Pneumomediastinum
- Pneumothorax
- Procedural complications
- Pseudo aneurysm or AV fistula at access site
- Sepsis
- Seroma
- Skin irritation
- Syncope
- Thrombosis / stenosis
- Tissue inflammation, fibrosis or damage
- Vessel occlusion
- Vessel wall damage / perforation
- Wound healing issues
- Wound infection / phlebitis

The potential complications associated with diaphragm or phrenic nerve stimulation are:

- Arrhythmia
- Bradycardia
- Diaphragm injury
- Discomfort
- Hypercapnia / hypocapnia
- Hypoxia
- Liberation of lung mucus plugs/secretions
- Muscle fatigue or discomfort
- Nerve injury
- Pain or discomfort during stimulation
- Inappropriate stimulation
- Phrenic nerve damage or injury
- Syncope

AeroPace System Overview and Setup

The AeroPace System (“System”) consists of six components. The AeroPace Neurostimulation Catheter may be placed in the left subclavian vein or left jugular vein. See the AeroPace Neurostimulation Catheter Kit Instructions for Use for details. The Console must always be operated under clinician supervision.

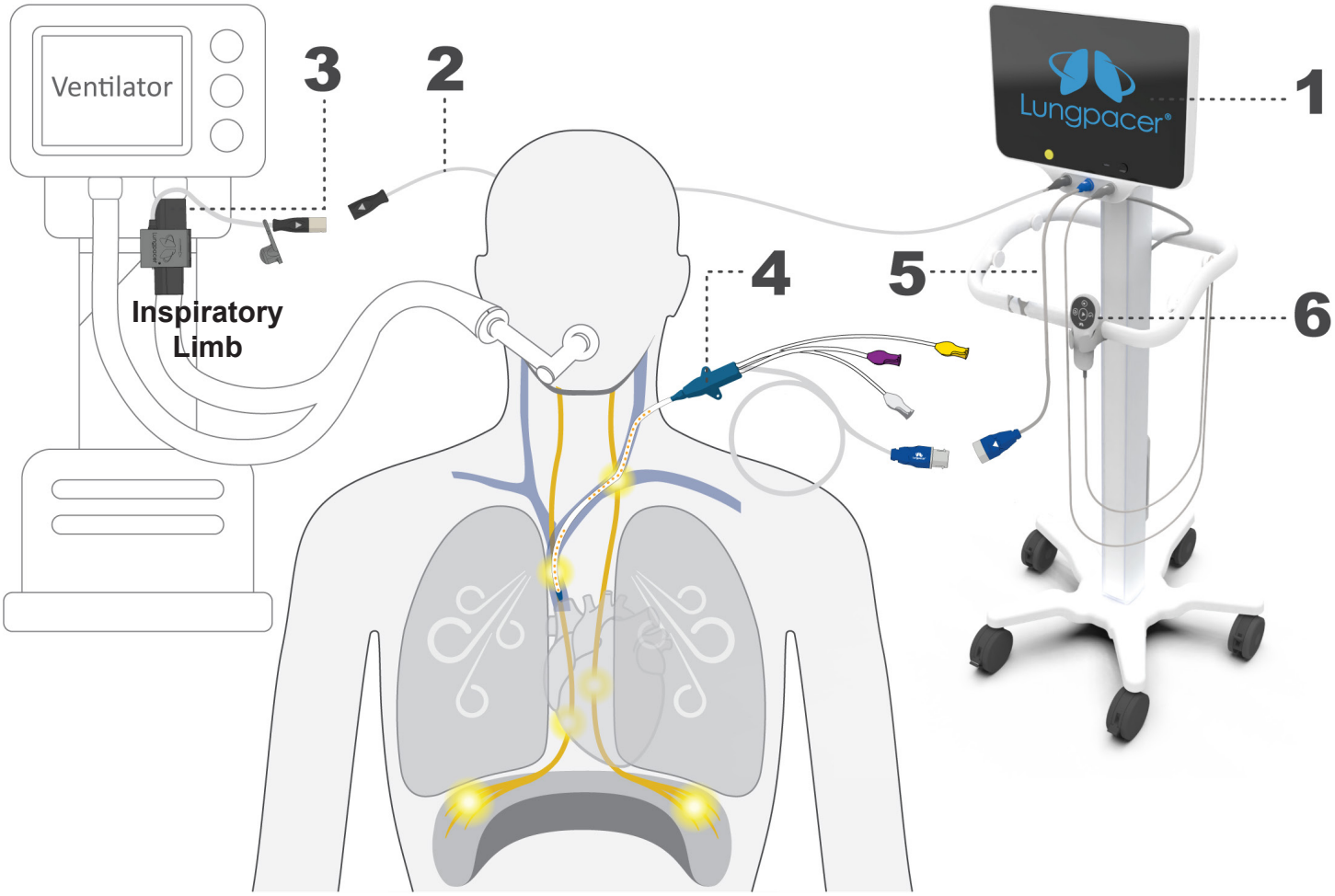
WARNING:

- Connect the Console power cord (the only means for mains disconnection) to an easily accessible “Hospital Only” or “Hospital Grade” AC mains outlet that is properly grounded with protective earth, and is compatible with the ratings printed on the Console label. Connecting the Console to an incompatible power source may result in fire or electrical shock.
- Do not modify the AeroPace System. Do not use or connect any devices to the AeroPace System or its components that are not described in this User Guide.
- The AeroPace System has not been evaluated for its interaction with all possible medical equipment under all operating conditions. Use of the AeroPace System outside of the Operating Conditions may result in injury. Do not use the AeroPace System with equipment likely to interact adversely with neurostimulation devices or central venous catheters. Assess all potential interactions before using the AeroPace System in conjunction with other medical equipment. Use of accessories other than those specified may result in increased electromagnetic emissions or decreased electromagnetic immunity.

CAUTION:

- Do not use or connect any devices to the AeroPace System or its components that are not described in these instructions.
- Do not use the AeroPace System or any of its components if they appear altered or damaged, or have exposed wires. Using damaged components may result in electrical shock.

Patient Setup and System Overview



1 Position the **Console**, typically on the same side of the patient as the Catheter insertion point (patient's left side), toward the head of the bed. Plug the console into hospital-grade wall power and lock its wheels prior to use. See *"AeroPace Neurostimulation Console" on page 10* for more information.

2 Use the **Airway Sensor Cable** with dark gray connectors to electrically connect the Airway Sensor to the Console.

3 Pneumatically connect the **Airway Sensor** between **inspiratory limb** of the patient's ventilator circuit and the ventilator.

4 The **AeroPace Neurostimulation Catheter** will be inserted into the patient's left subclavian vein, or left jugular vein.

5 Use the **Catheter Cable** with blue connectors to connect the patient's Catheter to the Console.

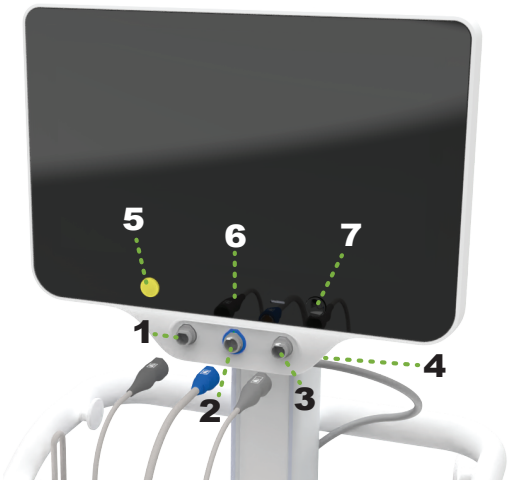
6 The **Handheld Controller** connects to the Console's right-most, light gray port.

AeroPace Neurostimulation Console

The AeroPace Neurostimulation Console (“Console”) generates stimulations that are delivered to the electrodes on the Catheter and result in contraction of the diaphragm. The Console has a touchscreen user interface and is mounted on the AeroPace Neurostimulation Console Cart (“Cart”) for mobility.

Assembling Console Components

To set up the Console, plug the dark gray Airway Sensor Cable connector, blue Catheter Cable connector, and light gray Handheld Controller connector into the Console’s front panel.



#	Item
1	Airway Sensor Cable connector (dark gray)
2	Catheter Cable connector (blue)
3	Handheld Controller connector (light gray)
4	Power cord connection (underneath the display)
5	Stop button: Forces an immediate shutdown of the Console (yellow)
6	Power indicator (illuminated blue when the Console is connected to power)
7	Power button (black)

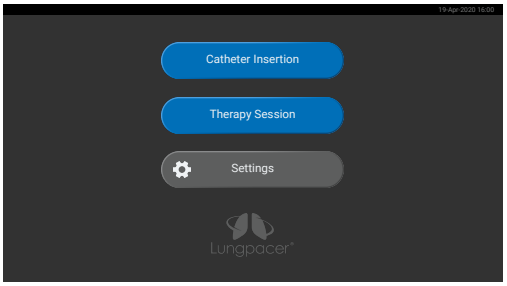
Positioning and Powering the Console

Position the Console based on room setup, typically on the same side of the patient as the Catheter insertion point (patient’s left side), toward the head of the bed. Ensure there is access to a hospital-grade AC receptacle that meets local requirements.

Press the **Power** button once to power the system on. The Lungpacer logo will display as the System starts.

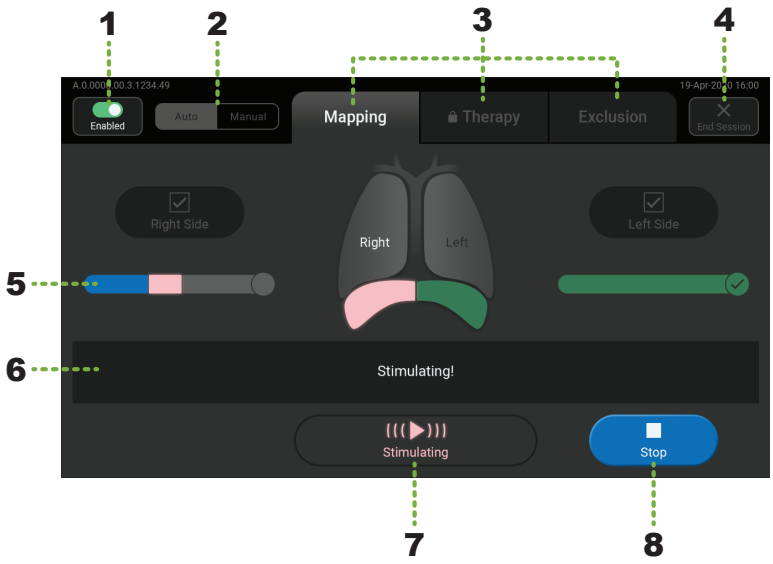
Touchscreen Navigation

The Home screen will appear after powering on the Console, with three options:



- **Catheter Insertion** is typically only used once per patient, during and immediately after the Catheter insertion procedure.
- **Therapy Session** is used to perform Mapping and deliver Therapy to the patient.
- **Settings** is used to adjust System parameters, such as the date and time (displayed in the upper right-hand corner of the Home screen) and language (including Dutch, English, French, German, Italian, Portuguese, and Spanish).

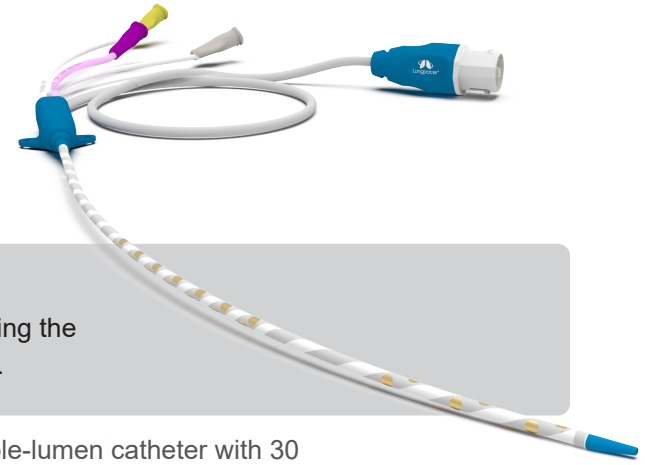
This annotated example of the Mapping screen illustrates some of the buttons and displays that are often available while using the System:



#	Item	Description
1	**Enable/ Disable**	Locks and unlocks the touchscreen and Handheld Controller.
2	**Auto/Manual**	Toggles between Auto (default) and Manual modes.
3	**Navigation Tabs**	When Therapy Session is selected from the Home Screen, the Mapping, Therapy, and Exclusion tabs will be displayed. Note that the Therapy tab will remain locked until Mapping is successful. When Catheter Insertion is selected from the Home screen, the ECG, Placement, and Exclusion tabs will be displayed.
4	**End Session**	When a Catheter Insertion or Therapy Session is complete, press this button to view information about the session before powering off the Console.
5	**Progress Bar**	The Progress Bar provides a visual estimate of process progression. It illuminates in different colors to indicate status: Analyzed (blue), Active (white), Stimulating (pink), Unsure (teal), Confirm (light green), and Complete (dark green).
6	**Notification Box**	Displays text on the lower portion of the touchscreen, including information about recent actions, instructions for using the System, warnings, and other notifications.
7	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during and between stimulations.
8	**Stop**	Stops the series of Stims that are in progress. Note that use of the on-screen blue Stop button will not shut down the System, but use of the yellow Stop button on the front of the Console will.

AeroPace Neurostimulation Catheter and Catheter Cable

The AeroPace Neurostimulation Catheter is intended for use with the AeroPace System for temporary transvenous diaphragm activation, and for short-term (< 30 days) central venous access for administering IV fluids, blood products, medications, and parenteral nutrition solutions, as well as blood withdrawal, central venous pressure monitoring, and power injection of contrast media.



⚠ **CAUTION:** Refer to the AeroPace Neurostimulation Catheter Kit Instructions for Use for warnings, cautions, and instructions regarding the insertion, removal, use, maintenance, and disposal of the Catheter.

The single-use AeroPace Neurostimulation Catheter is an 8.5Fr, 23cm triple-lumen catheter with 30 electrodes arranged in two arrays. The distal array of 9 electrodes is designed to capture the right phrenic nerve, and the proximal array of 21 electrodes is designed to capture the left phrenic nerve. The Catheter is inserted percutaneously over a guidewire used to facilitate access to the central venous system and can be placed in the left subclavian vein or left jugular vein.

The Catheter is provided sterile and is packaged in the AeroPace Neurostimulation Catheter Kit ("Catheter Kit") along with other single-use accessories required to complete the Catheter insertion procedure using the Seldinger technique. The Catheter Kit contents are listed below. Ancillary medical supplies such as saline flushes, local anesthetic, skin preparation materials, or sterile gloves are not included.

Note: The AeroPace Neurostimulation Catheter is not made with natural rubber latex.

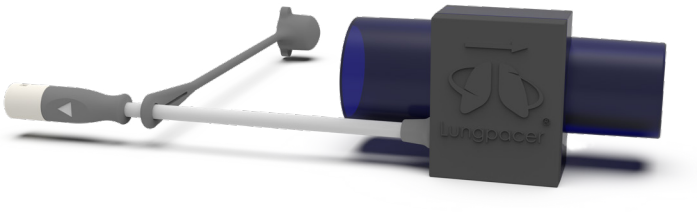
Catheter Kit Component	Qty	Catheter Kit Component	Qty
AeroPace Neurostimulation Catheter, 8.5Fr. (2.8mm) x 23cm	1	Primary Cable Clamp	1
Needle, 18G x 2.75in (1.3mm x 70mm)	1	Guidewire Tip Protector	1
Scalpel, #11	1	Dressing, Tegaderm, 4in x 4.75in (10cm x 12cm)	1
Sharps Receptacle	1	Gauze, 4in x 4in (10cm x 10cm)	5
Syringe, 3ml, Luer Lock with 25G x 1in (0.5mm x 25mm) Needle	1	Suture, 3-0 Silk, C7 Reverse Cutting Needle	1
Syringe, 5ml, Luer Slip	2	Drape, 24in x 36in (60cm x 90cm), with 4in (10cm) Fenestration	1
Needle-Free Male Luer Lock Injection Site	3	Catheter Clamp Fastener	1
Guidewire Dispenser	1	Guidewire J-Tip, EHD 0.032in (0.81mm) x 70cm	1
Guidewire J Straightener	1	Dilator, 8Fr. x 4in (2.7mm x 10cm)	1
Catheter Clamp	1	Needle Holder, 5in (13cm)	1

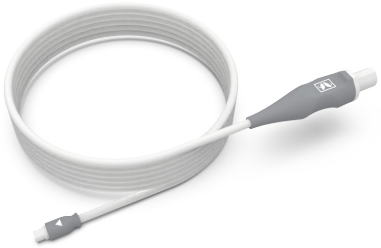
When connected to the Catheter, the AeroPace Catheter Cable ("Catheter Cable") conducts stimulations ("Stims") from the Console to the Catheter's electrodes. When not in use, the Catheter Cable should be disconnected from the Catheter, but may remain plugged into the Console's front panel.

AeroPace Airway Sensor and Airway Sensor Cable

The AeroPace Airway Sensor (“Airway Sensor”) is required for use of the System in Auto mode. It provides input about airway pressure and the patient’s breathing cycle to the Console.

The Airway Sensor connects pneumatically to the patient’s ventilator circuit between the inspiration limb of the circuit and the ventilator connection. Alternatively, it may be placed between the Y-piece and the patient’s endotracheal or tracheostomy tube using an airway adapter. It connects to the Console electrically by way of the AeroPace Airway Sensor Cable (“Airway Sensor Cable”). When not in use, the Airway Sensor Cable should be disconnected from the Airway Sensor, but may remain plugged into the Console’s front panel.





AeroPace Handheld Controller

When connected to the Console, the AeroPace Handheld Controller (“Handheld Controller”) allows the clinician to activate specific functions remotely, beyond arm’s reach of the Console’s touchscreen. During use, the Lungpacer logo illuminates to indicate that the Handheld Controller is connected to the powered Console.

Catheter Insertion

WARNING:

- Do not position the Catheter (or allow it to remain) in the right atrium, right ventricle, or in a position that may induce cardiac arrhythmia. Incorrect positioning of the Catheter may result in cardiac injury, arrhythmia, or cardiac tamponade leading to severe injury or death.
- The AeroPace ECG feature is intended to function as an assistive aid in the placement of the AeroPace Neurostimulation Catheter. Do not use the AeroPace ECG feature to diagnose cardiac events or diseases.

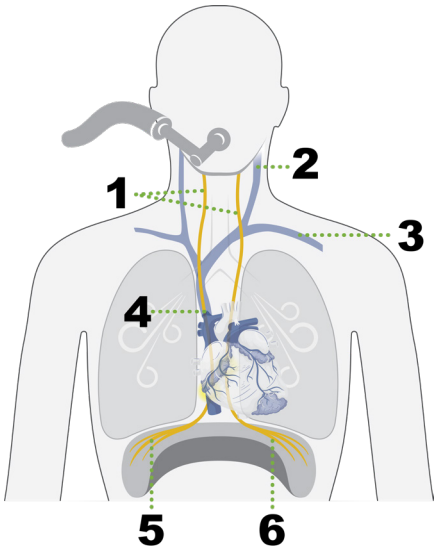
CAUTION:

- Refer to the AeroPace Neurostimulation Catheter Kit Instructions for Use for warnings, cautions, and instructions regarding the insertion, removal, use, maintenance, and disposal of the Catheter.
- When disconnected, ensure all Catheter and Catheter Cable connector pins are not in contact with the operator, or with any other active or electrically grounded surface. Touching or electrically grounding the contacts of the Catheter's electrical connector (including the contacts of the Catheter Cable connector while connected to the Catheter) may result in cardiac arrhythmia.
- Improper handling of the Catheter extension lines and/or the insertion site, use of a non-sterile Catheter, use of the Catheter beyond its recommended use period (30 days), and/or failure to adhere to aseptic catheter insertion technique may result in infection.
- Multiple replacements of the Catheter increase the risk of vessel wall damage and perforation.
- Excessive bending, torquing, or kinking of the Catheter may cause damage to the device including its electrical conductors.
- Damage to the Catheter or occlusion of any of its lumens may increase the risk of embolism.

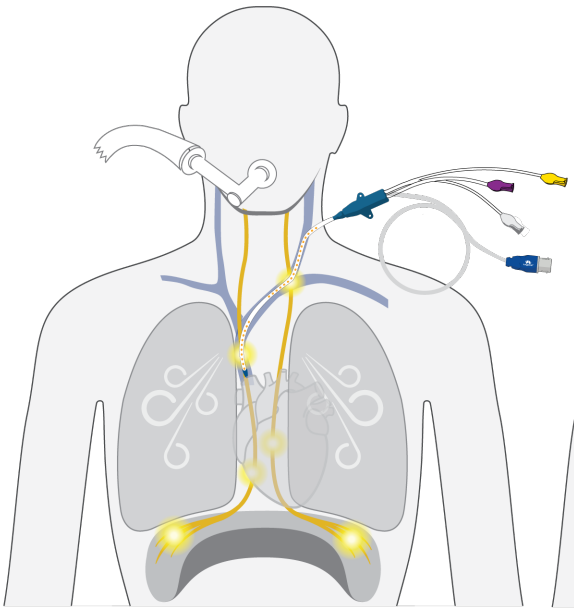
Step 1: Plan the Insertion

Prepare the patient for AeroPace Neurostimulation Catheter insertion according to your institutional guidelines, just as you would for insertion of a central venous catheter. The Catheter may be placed into the left subclavian vein or left jugular vein using the Seldinger technique. The Catheter tip must be located on the right side of the mediastinum in the superior vena cava (SVC) above its junction with the right atrium and parallel to the vessel wall, and its distal tip positioned at a level above either the azygous vein or the carina of the trachea, whichever is better visualized. Judge the vein access point based on patient anatomy.

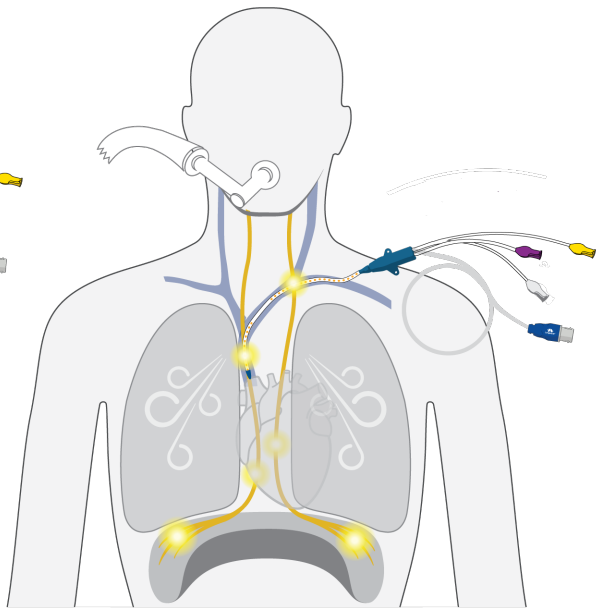
⚠ **CAUTION:** The US Centers for Disease Control and Prevention recommends Catheter placement using a subclavian site rather than a jugular site in adult patients to minimize infection risk.



#	Anatomy
1	Phrenic Nerves
2	Left Jugular Vein
3	Left Subclavian Vein
4	Superior Vena Cava (SVC)
5	Right Hemidiaphragm
6	Left Hemidiaphragm



Jugular Catheter Insertion



Subclavian Catheter Insertion

Step 2: Gather Supplies and Clinical Assistance

Gather items needed at the patient's bedside at the time of the Catheter insertion procedure, including:

- Console, assembled with the Airway Sensor Cable, Catheter Cable, and Handheld Controller
- New Airway Sensor
- Catheter Kit: See *"AeroPace Neurostimulation Catheter and Catheter Cable" on page 12* for a full list of kit components
- Any additional supplies not provided in the Catheter Kit, including saline flushes, local anesthetic, skin preparation materials, sterile gown and gloves, or other preferred supplies
- Clinical assistant to operate the Console outside of the sterile field

⚠ **CAUTION:** Inspect the Catheter Kit expiration date before use. Use of expired product may lead to injury.

Step 3: Set Up the Airway Sensor

Connect a new Airway Sensor to the patient's ventilator airway circuit prior to setting up the sterile field for the Catheter insertion procedure. To connect an Airway Sensor to the patient's ventilator circuit:

1. Inspect the Airway Sensor packaging before opening it, and then remove and inspect the Airway Sensor. Only use the Airway Sensor if it and its packaging are intact, clean, and undamaged.
2. Before breaking the patient's ventilator circuit, position the Airway Sensor so that the arrow points toward the patient.
3. Position the Airway Sensor between the inspiration limb of the circuit and the ventilator connection.

   Note: The Airway Sensor may also be positioned between the Y-piece and the patient's endotracheal or tracheostomy tube using an airway adapter (e.g., HMEF). If positioned at the Y-piece, the Airway Sensor will add approximately 13 ml of dead space to the airway circuit.

4. Disconnect the patient's ventilator circuit at the location the Airway Sensor will be installed, and then quickly connect the Airway Sensor and reconnect the circuit.
5. When the ventilator circuit is reestablished, ensure that the patient's breathing returns to a stable pattern.

Note: The Airway Sensor is designed to remain connected to the patient's ventilator circuit between Therapy Sessions, for a maximum of 30 days.

Step 4: Prepare the Console

Prepare the Console for use during and immediately after the Catheter insertion process:

1. Position the Console based on room setup, typically on the same side of the patient as the Catheter insertion point (patient's left side), toward the head of the bed. Ensure there is access to a hospital-grade AC receptacle that meets local requirements.
2. Plug the Console into wall power.
3. Lock the Cart's wheels.
4. Power on the Console by pressing the **Power** button.

Step 5: Insert the Catheter

To insert the Catheter:

1. Prepare the patient for the Catheter insertion procedure.

> Note: The Console has an ECG feature that can be used to help guide the insertion of the Catheter. See *"Using the ECG Feature" on page 18* for details.

2. Insert the AeroPace Neurostimulation Catheter via the left subclavian vein or left jugular vein using the Seldinger technique, following your institution's guidelines. **Follow all instructions in the AeroPace Neurostimulation Catheter Kit Instructions for Use.**

⚠ **CAUTION:**
- Improper vein access technique may result in vessel wall damage or perforation.
- Observe the patient closely for unwanted effects during the Catheter insertion and Placement process. Incorrect positioning of the Catheter's electrodes may result in pain or discomfort from stimulation of unintended nerves or tissue.

3. Advance and retract the Catheter as needed so that its tip is in the distal SVC.

⚠ **CAUTION:** Ensure that the heart rhythm is not affected when the Catheter is being advanced. If an atrial arrhythmia is detected that could be produced by the Catheter tip having entered the atrium, retract the Catheter tip back into the SVC.

Using the ECG Feature

WARNING: The AeroPace ECG feature is intended to function as an assistive aid in the placement of the AeroPace Neurostimulation Catheter. Do not use the AeroPace ECG feature to diagnose cardiac events or diseases.

If the ECG feature will be used while placing the Catheter:

1. Following your institutional guidelines for maintaining the sterile field and sterility of the Catheter, have a clinical assistant connect the Catheter's electrical connector to the Catheter Cable.

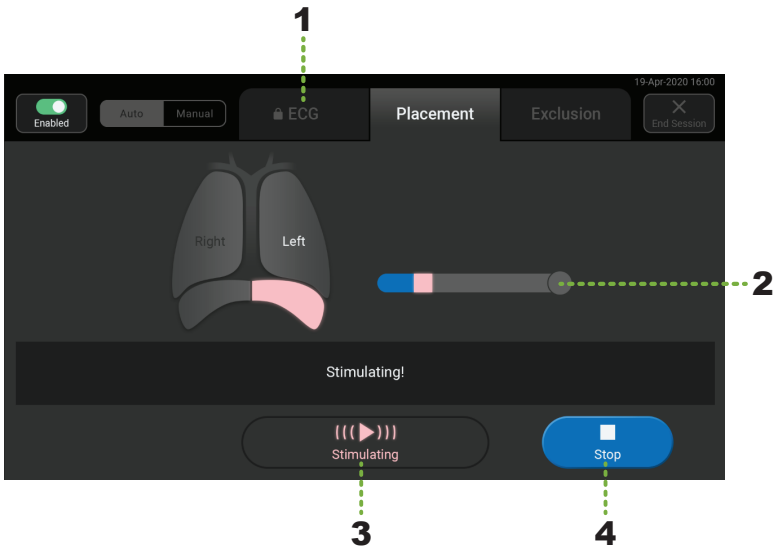
2. From the Console's Home screen, have the clinical assistant select **Catheter Insertion**, and then the **ECG** tab.

3. While maintaining the sterile field, insert the Catheter. As the Catheter is advanced into the superior vena cava (SVC) and retracted, the intravascular electrogram signal will change in amplitude and morphology. Observe and monitor the displayed signal as an indicator of Catheter position. Inverted electrogram morphology may indicate that the Catheter is over-inserted and has entered the right atrium. If so, retract the Catheter slowly until a normal electrogram signal is restored.

Note: It may be useful to compare the electrogram of the Catheter inserted at two different depths. The strip on the upper portion of the screen will display the real-time electrogram, and the lower strip will display the electrogram from the previous 10 seconds. The real-time data on the upper strip can be captured by pressing the **Snapshot** button to the left of the strip. The displayed data will be frozen and displayed on the lower strip, while the upper strip continues to display the real-time electrogram. By comparing the real-time electrogram in the upper strip with the frozen snapshot below it, the electrogram characteristics at two different Catheter positions can be assessed and compared. Press the **Go Live** button at any time to release the captured electrogram snapshot on the lower strip.

Step 6: Placement

Once the Catheter's distal tip is in the correct position, use the Placement tab on the Catheter Insertion screen to verify that the AeroPace Neurostimulation Catheter's left-side electrodes are stimulating the patient's left phrenic nerve. The Placement screen includes the following features:



#	Item	Description
1	**ECG Tab**	Displays the optional intravascular electrogram (ECG) feature that can be used to help guide the insertion of the AeroPace Neurostimulation Catheter.
2	**Progress Bar**	The Progress Bar provides a visual estimate of process progression. It illuminates in different colors to indicate status: Analyzed (blue), Active (white), Stimulating (pink), Unsure (teal), Confirm (light green), and Complete (dark green).
3	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during and between stimulations.
4	**Stop**	Stops the series of Stims that are in progress. Note that use of the on-screen blue Stop button will not shut down the System, but use of the yellow Stop button on the front of the Console will.

To perform Placement:

1. Once the System is ready and the **Stimulate** button turns blue, press it. Placement will proceed automatically, as indicated by the progress bar on the screen.
2. Once Placement verification completes successfully, lightly secure the Catheter using a clamp or other temporary means. This will prevent Catheter dislodgement or movement before its position is confirmed in the next step.

Note: If Placement verification is unsuccessful, you may try again in Auto mode, or try completing the procedure using Manual mode, instead. See *"Manual Placement" on page 26* for details.

3. Press **Continue**.
4. If you are done using the Console, press **End Session**. Always disconnect the electrical cable connectors at the Catheter and Airway Sensor before pressing the **Power** button to turn off the Console. If Therapy will be delivered immediately after Placement, keep the System powered on and its cables connected.

Note: If needed, the Exclusion tab can be used to identify and exclude specific electrodes that cause unwanted patient effects. See "*"Electrode Exclusion" on page 31* for details.

Step 7: Confirm Distal Tip Position

Follow institutional guidelines (such as chest x-ray) to confirm the Catheter tip is positioned in the SVC. Once confirmed, secure the Catheter manifold to the patient's skin according to your institution's guidelines.

⚠ **CAUTION:** Secure the Catheter to prevent movement after Placement has completed successfully. Movement of the Catheter during Therapy may result in inappropriate Therapy or overstimulation and injury of the diaphragm.

Therapy Sessions

Therapy delivered from the AeroPace System is modeled on classic muscle rehabilitation therapy consisting of exercise, rest, and exercise again to build muscle strength. Each patient receiving Therapy is advanced through the progressive diaphragm strengthening regimen at their own pace, moving to the next step based on individual performance, comfort, and ventilator settings. Optimize Therapy at each session based on patient comfort.

WARNING:

- Ventilator settings should be configured appropriately for the patient according to institutional guidelines. Observe the patient closely during System use to ensure that the ventilator settings and the AeroPace System settings are compatible. Failure to do so may result in inadequate ventilation, ventilator dyssynchrony, inappropriate Therapy delivery, or lung or diaphragm injury. See *"Therapy" on page 23* for details.
- Delivery of electrical stimulation in the right atrium, right ventricle, or other positions may result in cardiac arrhythmia. If unwanted patient effects (such as an arrhythmia) occur during Mapping or Therapy, stop stimulation immediately. If needed, perform Exclusion before restarting Mapping or Therapy. See *"Electrode Exclusion" on page 31* for details.
- The AeroPace Neurostimulation Catheter is MR Conditional, but the Neurostimulation Console is MR Unsafe. Conditions under which the AeroPace Neurostimulation Catheter is MR compatible and may be scanned safely are described in the Catheter Kit Instructions for Use. Always disconnect the Catheter from the Neurostimulation Console before conducting MRI, and keep the Console away from MR equipment.

Setup

To provide Therapy to the patient, begin by preparing the Console for use:

1. Position the Console based on room setup, typically on the same side of the patient as the Catheter insertion point (patient's left side), toward the head of the bed. Ensure there is access to a hospital-grade AC receptacle that meets local requirements.
2. Plug the Console into wall power.
3. Lock the Cart's wheels.
4. Power on the Console by pressing the Power button.
5. Connect the Airway Sensor to the Airway Sensor Cable and connect the Catheter to the Catheter Cable.

Mapping

Mapping identifies which of the AeroPace Neurostimulation Catheter's 30 electrodes are suitable for use during Therapy, and at what baseline Therapy Levels. Baseline Therapy Levels differ from patient to patient, and may also differ for the same patient from one Therapy session to another. For this reason, Mapping must be performed before every Therapy session. Each hemidiaphragm is mapped individually, so that Therapy can be optimized on each side.

#	Item	Description
1	**Hemidiaphragm Selector**	The hemidiaphragm buttons select the sides (left and/or right) that will be Mapped.
2	**Progress Bar**	The Progress Bar provides a visual estimate of process progression. It illuminates in different colors to indicate status: Analyzed (blue), Active (white), Stimulating (pink), Unsure (teal), Confirm (light green), and Complete (dark green).
3	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during and between stimulations.
4	**Stop**	Stops the series of Stims that are in progress. Note that use of the on-screen blue Stop button will not shut down the System, but use of the yellow Stop button on the front of the Console will.

To perform Mapping:

1. Select **Therapy Session** from the Home screen, and then select the **Mapping** tab.
2. Ensure Right Side and Left Side are both checked, unless clinical conditions do not allow Therapy to be delivered on both hemidiaphragms. To omit a side from Mapping and Therapy, deselect it by clicking on the corresponding hemidiaphragm's checkmark.

   Note: At least one side must be successfully Mapped before the Therapy tab is unlocked for use.
3. Press **Stimulate**. The progress bar(s) and notification box will show the status of the Mapping process.

   Note: If needed, stop the delivery of stimulations at any time by pressing the blue Stop button on the touchscreen or Handheld Controller.
4. When Mapping is successful for the selected side(s), the 'lock' icon on the Therapy tab will disappear. Press **Continue** to proceed with Therapy.

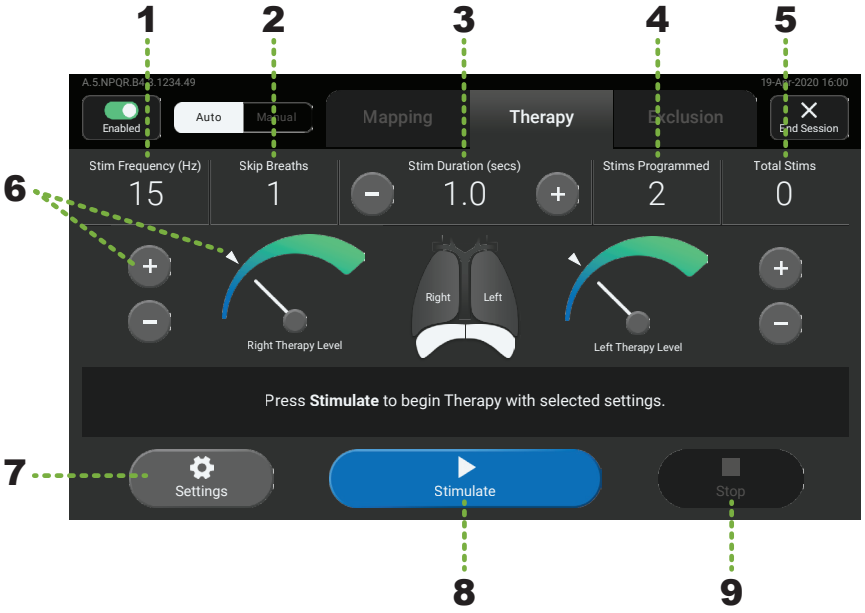
   Note: If Mapping is unsuccessful on one or both sides, press **Continue**. The Mapping tab will remain active, where you can try Auto Mapping again, or press the **Manual** toggle to troubleshoot further by performing Mapping manually. See *"Electrode Exclusion" on page 31* for details. Therapy will only be delivered to successfully mapped side(s).

Therapy

The Therapy tab will unlock after successful Mapping on at least one side.

Daily therapy is delivered in two sessions, spaced at least three hours apart. Each session includes 60 stimulations, for a total of 120 stimulations each day.

Optimizing Therapy entails delivering the target number of Stims at the maximum Therapy Level possible based on patient comfort during both daily Therapy sessions.



To maximize diaphragm strengthening, do not skip Therapy Sessions.

Before delivering Therapy, familiarize yourself with the screen and adjust the parameters appropriately for the patient:

#	Item	Description	Range	Default
1	**Stim Frequency (Hz)**	Use only the default Stim Frequency setting of 15 Hz. This is the pulse repetition rate within each Stim.	See specs	15 Hz
2	**Skip Breaths**	How many patient breaths occur between each Stim. A setting of 1 is appropriate for most patients (meaning a Stim is delivered every other breath) but may need to be adjusted for patients with a rapid respiratory rate, when a persistent Early Breath Detected system message is displayed, or when patient comfort is negatively impacted. Increasing the Skip Breaths setting will allow more breaths to occur between each Stim. Press Settings and then press the plus (+) and minus (−) buttons to adjust Skip Breaths.	1 – 5	1
3	**Stim Duration**	The length of time over which a Stim is delivered. Increase the Stim Duration to the maximum of 1.2 seconds, if possible. Adjusting ventilator settings may be required so that the patient's inspiratory time is as close as possible to the Stim Duration. Press the plus (+) and minus (−) buttons to adjust the Stim Duration.	0.1 – 1.2	1.0
4	**Stims Programmed**	The number of Stims that will be delivered each time the Stimulate button is pressed. Press Settings and then press the plus (+) and minus (−) buttons to adjust the Stims Programmed.	1 – 10	2
5	**Total Stims**	The total number of Stims delivered within the Therapy Session.	n/a	n/a
6	**Therapy Levels (Right and Left)**	The strength (or "intensity") of each Stim. To optimize diaphragm contraction, increase Therapy Levels to the maximum possible based on patient comfort during each session. The white arrows on the display indicate the baseline Therapy Levels that were established for each side during Mapping. Note that setting the Therapy Level too far below its baseline may deliver Stims at a sub-therapeutic level. Press the plus (+) and minus (−) buttons to adjust the Therapy Level for each side (right and left) independently.	Min – Max	Baseline Therapy Level
7	**Settings**	The Settings button opens a screen where additional Therapy parameters can be configured.	n/a	n/a
8	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during and between stimulations.	n/a	n/a
9	**Stop**	Stops the series of Stims that are in progress. Note that use of the on-screen blue Stop button will not shut down the System, but use of the yellow Stop button on the front of the Console will.	n/a	n/a

⚠ **CAUTION:**

- Ensure Therapy is provided with the regularity and settings appropriate for the patient and their condition. Delivery of more than 120 stimulations per day was not studied in clinical trials.
- Therapy delivered from the AeroPace System may result in the liberation of mucus and/or secretions. Monitor airway secretions and suction as needed during and after Therapy to help avoid airway occlusion.

To deliver Therapy:

1. Adjust the initial Therapy session parameters as appropriate for the patient.
2. Press **Stimulate** and observe the patient for diaphragm contraction and signs of discomfort.

   Note: If needed, stop the delivery of stimulations at any time by pressing the blue Stop button on the touchscreen or Handheld Controller.

3. After the configured number of Stims Programmed have been delivered, adjust the **Therapy Levels** and any other parameters as needed to optimize Therapy.

   Note: The purpose of adjusting the Therapy Levels after each round of Stims is to optimize Therapy by reaching the maximum level possible in accordance with patient comfort.

4. Repeat steps 2 and 3 until the optimal Therapy Levels for the session are established.
5. Provide the desired number of Total Stims to the patient by pressing **Stimulate** as needed. You may optionally press **Settings** and increase the **Stims Programmed** to a higher value, so that more stimulations are delivered every time the Stimulate button is pressed.
6. Always continue to assess the patient during Therapy. When Total Stims reaches 60, press **End Session**. A Summary screen will appear with information about the Therapy session.
7. Always disconnect the electrical cable connectors at the Catheter and Airway Sensor after use. The cables may remain connected to the Console.
8. Press the **Power** button to turn off the Console.

Note: A second daily Therapy session should be provided at least 3 hours later, following these same instructions.

Manual Mode

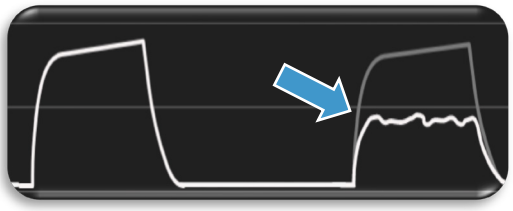
WARNING:

- Do not position the AeroPace Neurostimulation Catheter (or allow it to remain) in the right atrium, right ventricle, or in a position that may induce cardiac arrhythmia. Incorrect positioning of the Catheter may result in cardiac injury, arrhythmia, or cardiac tamponade leading to severe injury or death.
- Ventilator settings should be configured appropriately for the patient according to institutional guidelines. Observe the patient closely during System use to ensure that the ventilator settings and the AeroPace System settings are compatible. Failure to do so may result in inadequate ventilation, ventilator dyssynchrony, inappropriate Therapy delivery, or lung or diaphragm injury. See *"Therapy" on page 23* for details.
- The AeroPace Neurostimulation Catheter is MR Conditional, but the Neurostimulation Console is MR Unsafe. Conditions under which the AeroPace Neurostimulation Catheter is MR compatible and may be scanned safely are described in the Catheter Kit Instructions for Use. Always disconnect the Catheter from the Neurostimulation Console before conducting MRI, and keep the Console away from MR equipment.

In some cases, Manual mode may be useful in troubleshooting Placement, Mapping, or Therapy.

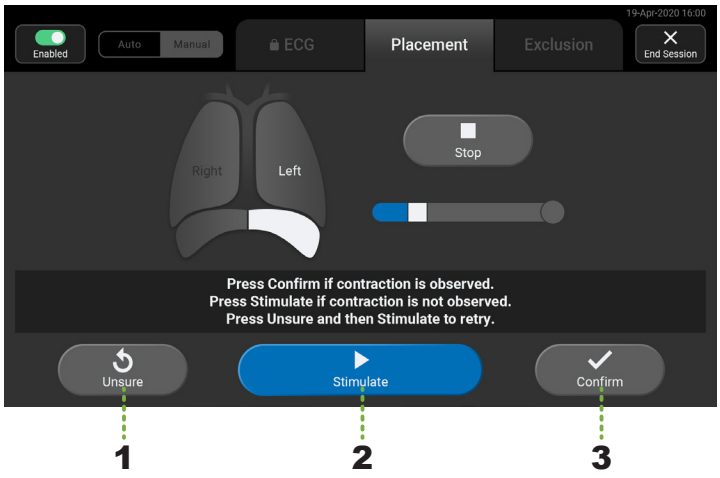
Using the System in Manual mode does not require use of an Airway Sensor. Instead, the System relies on the clinician to carefully observe the patient and ventilator waveforms during each Stim in Placement and Mapping, and then provide feedback to the Console. Contractions typically cause deflections on the ventilator waveforms, as shown in the image below.

When providing Therapy in Manual mode, the System relies on the clinician to press the Stimulate button at the end-expiratory phase of the patient's breathing cycle to deliver Stims. The clinician must also precisely set parameters such as Stim Rate appropriately for the patient's ventilator settings and breathing patterns to avoid ventilator dyssynchrony.



Manual Placement

During manual Placement, the clinician palpates the left hemidiaphragm and/or observes the ventilator for deflections on the pressure and flow waveforms, and provides input to the Console about whether a diaphragm contraction occurred as a result of Stims from AeroPace Neurostimulation Catheter electrode combinations. After the Catheter is inserted, two clinicians are needed to perform manual Placement: One inside the sterile field to observe and palpate the patient, and one outside it to operate the Console.



Manual mode requires that the clinician provide feedback to the Console using the three buttons on the bottom portion of the screen:

#	Item	Description
1	**Unsure**	Use the Unsure button to indicate uncertainty about whether diaphragm contraction occurred during a Stim. It will prompt the Console to program a Stim with the same electrode combination and intensity again.
2	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during stimulations.
3	**Confirm**	Use the Confirm button to indicate that a diaphragm contraction was observed during a Stim.

To perform manual Placement:

1. Select **Catheter Insertion** from the Console's Home Screen, ensure the **Placement** tab is selected, and then toggle to **Manual** mode.
2. Have a clinician inside the sterile field prepare to observe diaphragm contractions by placing one hand on the patient's lower ribcage to palpate and/or by observing the pressure and flow waveforms on the mechanical ventilator.
3. Have an assistant outside the sterile field press **Stimulate** at end-expiration, while the clinician inside the sterile field palpates the patient's hemidiaphragm and/or observes the ventilator's waveforms.

> Note: Contractions are typically easiest to observe when Stims are delivered during the end-expiration period of the patient's respiratory cycle. Because contractions will only be observed for the electrode combinations nearest to the phrenic nerve, it is normal to not detect a contraction from some Stims during this process.

4. After the Stim is complete, provide feedback to the Console by indicating whether a diaphragm contraction was observed:
   - If you are not sure, select **Unsure** to select the same electrodes and intensity again.
   - If contractions occurred, select **Confirm**.
   - If there was no contraction, do not select either button. It is normal and an expected part of the process to not detect a contraction during a Stim and to move on to the next electrode and intensity combination.

5 Repeat steps 3 and 4, following the instructions in the Notification Box, until all electrodes and intensities have been evaluated. Then, press **Complete**.

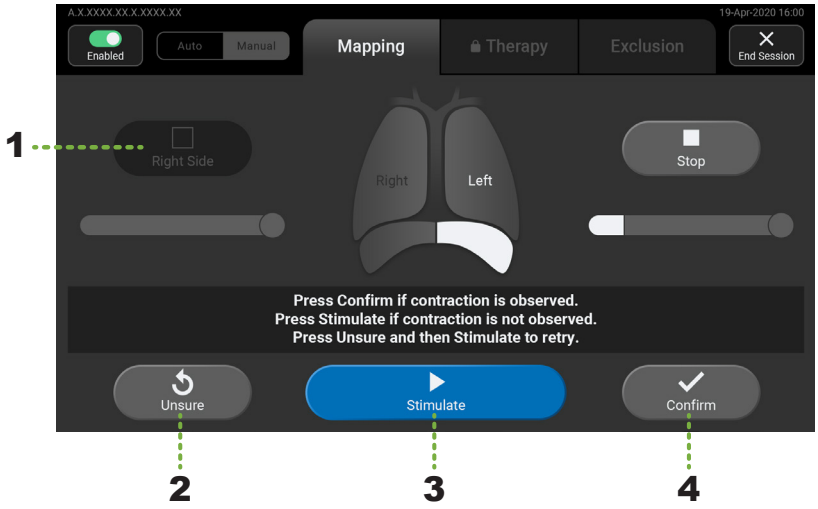
> Note: If no contractions are observed during the Placement verification process, it will be considered unsuccessful. If this occurs persistently, the Catheter may need to be repositioned. Refer to the AeroPace Neurostimulation Catheter Kit Instructions for Use for details. Once the Catheter is repositioned, try Placement again.

6 Press **Continue**.

7 If you are done using the Console, press **End Session**. Always disconnect the electrical cable connectors at the Catheter and Airway Sensor before pressing the **Power** button to turn off the Console. If Therapy will be delivered immediately after Placement, keep the System powered on and its cables connected.

Manual Mapping

The Mapping process identifies which of the AeroPace Neurostimulation Catheter's 30 electrodes are best suited for use during Therapy, and at what Therapy Levels. During manual Mapping, the left and right hemidiaphragms are palpated individually and/or the ventilator pressure and flow waveforms are observed for deflections that indicate diaphragm contraction. Input is provided to the Console to indicate whether a diaphragm contraction occurred as a result of Stims from Catheter electrode combinations.



Manual Mapping requires clinician feedback to the Console by way of three buttons on the bottom portion of the screen:

#	Item	Description
1	**Hemidiaphragm Selector**	The hemidiaphragm buttons select the side (left or right) that will be Mapped.
2	**Unsure**	Use the Unsure button to indicate uncertainty about whether diaphragm contraction occurred during a Stim. It will prompt the Console to program a Stim with the same electrode combination and intensity again.
3	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during stimulations.
4	**Confirm**	Use the Confirm button to indicate that a diaphragm contraction was observed during a Stim.

To perform manual Mapping:

1. Select **Therapy Session** from the Console's Home Screen, ensure the **Mapping** tab is selected, and toggle to **Manual** mode.

2. Leave Left Side checked to map the left hemidiaphragm, or check Right Side to map the right hemidiaphragm.

> Note: When Mapping in Manual mode, only one hemidiaphragm can be mapped at a time.

3. Prepare to observe diaphragm contractions by placing one hand on the patient's lower ribcage to palpate and/or by observing the pressure and flow waveforms on the mechanical ventilator. The screen will indicate when Mapping can begin.

4. Press **Stimulate** at end-expiration, while palpating the patient's hemidiaphragm and/or observing the ventilator's waveforms.

> Note: Contractions are typically easiest to observe when Stims are delivered during the end-expiration period of the patient's respiratory cycle. Because contractions will only be observed for the electrode combinations nearest to the phrenic nerve, it is normal to not detect a contraction from some Stims during this process.

5. After the Stim is complete, provide feedback to the Console by indicating whether a diaphragm contraction was observed:

   - If you are not sure, select **Unsure** to select the same electrodes and intensity again.
   - If contractions occurred, select **Confirm**.
   - If there was no contraction, do not select either button. It is normal and an expected part of the process to not detect a contraction during a Stim and to move on to the next electrode and intensity combination.

6. Repeat steps 4 and 5, following the instructions in the Notification Box, until mapping completes for the selected hemidiaphragm (right or left).

7. If desired, repeat steps 4 through 6 for the other hemidiaphragm (right or left), and then press **Continue**. The Therapy screen will be displayed, with Auto mode enabled.

> Note: To provide Therapy on only one hemidiaphragm, press the Therapy tab after the desired side is mapped.

> Note: If manual Mapping is unsuccessful on one or both sides, troubleshoot further by adjusting the patient's position (e.g., positioning the patient at the top of the bed to remove a bend in the torso, changing their posture, modifying the incline of the bed, or using or removing a pillow under a shoulder) and then repeat Mapping. If it is still unsuccessful on both sides, evaluate and consider altering the positioning of the Catheter. At least one side must be successfully Mapped before proceeding to Therapy.

Manual Therapy

Once Mapping has completed successfully on at least one side, Therapy can be initiated. When providing Therapy in Manual mode, the System relies on the clinician to press the Stimulate button at end-expiration of the patient's breathing cycle to deliver Stims. The clinician must also precisely set parameters such as Stim Rate and Stim Duration as needed for the patient's ventilator settings and breathing patterns to avoid ventilator dyssynchrony.

Therapy is delivered daily in two sessions, spaced at least three hours apart. Each session includes 60 stimulations, for a total of 120 stimulations each day.

Before delivering Therapy, adjust parameters appropriately for the patient.

Note: For a description of Stim Duration, Total Stims, Therapy Levels, and other on-screen buttons and displays, see *"Therapy" on page 23.*

⚠ CAUTION:

- Ensure Therapy is provided with the regularity and settings appropriate for the patient and their condition. Delivery of more than 120 stimulations per day was not studied during clinical trials.
- Therapy delivered from the AeroPace System may result in the liberation of mucus and/or secretions. Monitor airway secretions and suction as needed during and after Therapy to help avoid airway occlusion.

To deliver manual Therapy:

1. Adjust the initial Therapy session settings as appropriate for the patient, including the **Stim Duration** and the **Therapy Levels**.
2. Press **Stimulate** at end-expiration and observe the patient.

   WARNING: Delivery of electrical stimulation in the right atrium, right ventricle, or other positions may result in cardiac arrhythmia. If unwanted patient effects (such as an arrhythmia) occur during Mapping or Therapy, stop stimulation immediately. If needed, perform Exclusion before restarting Mapping or Therapy. See *"Electrode Exclusion" on page 31* for details.

   Note: If needed, stop the delivery of stimulations at any time by pressing the pressing the blue **Stop** button on the touchscreen or Handheld Controller.
3. Adjust the **Therapy Levels** and any other parameters as needed to optimize Therapy.

   Note: The purpose of adjusting the Therapy Levels after each round of Stims is to optimize Therapy by reaching the maximum level possible in accordance with patient comfort.
4. Repeat steps 2 and 3 until the optimal Therapy Levels for the session are established.

5 You may optionally press **Settings** and increase the **Number of Stims** to a higher value, while also carefully setting the **Stim Rate** appropriately for the patient's ventilator settings and breathing patterns.

Item	Description	Range	Default
Stim Rate	How many Stims are delivered per minute. Press the plus (+) and minus (–) buttons to configure a value appropriate for the patient's ventilator settings and breathing patterns, between 8 and 15 Stims per minute (in increments of 1). Note: When the Number of Stims is set to a value greater than 1 (one), Stims will be delivered according to the configured Stim Rate. Because the System does not automatically detect patient breathing in Manual mode, you must precisely set the Stim Rate to synchronize with the mechanical ventilator settings, and with the patient's intrinsic breathing patterns.	8 – 15	8
Stims Programmed	The number of Stims delivered (at the set Stim Rate) each time the Stimulate button is pressed. Press the plus (+) and minus (–) buttons to configure a value between 1 and 10 Stims (in increments of 1). Note: Unless you have precisely configured the Stim Rate to synchronize with the patient's mechanical ventilator settings, keep the Number of Stims set to 1, so that stimulations can be manually timed with the patient's breathing patterns.	1 – 10	1

6 Always continue to assess the patient during Therapy. When Total Stims reaches 60, press **End Session**. A Summary screen will appear with information about the Therapy session.

7 Always disconnect the electrical cable connectors at the Catheter and Airway Sensor (if connected) after use. The cables may remain connected to the Console.

8 Press the **Power** button to turn off the Console.

Troubleshooting

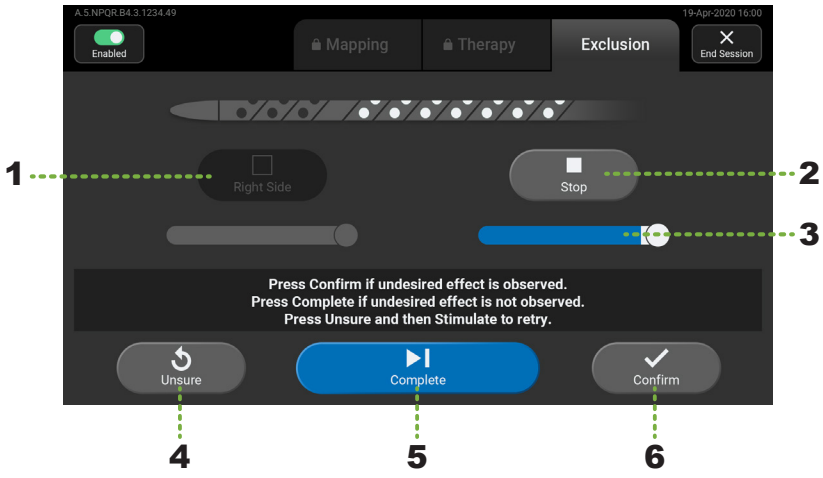
Electrode Exclusion

In some cases, it's possible for the Catheter's electrodes to cause unwanted effects.

WARNING: Delivery of electrical stimulation in the right atrium, right ventricle, or other positions may result in cardiac arrhythmia.

Use the Exclusion tab to identify and then temporarily disable (exclude) the specific Catheter electrodes that cause unwanted effects.

The Console will send Stims to one electrode combination at a time. The clinician must observe the patient closely to determine whether that electrode combination caused an unwanted effect, and then provide observational feedback to the Console. In this way, the electrodes that cause unwanted effects are identified and disabled.



#	Item	Description
1	**Side Selector**	Selects which grouping of Catheter electrodes (left or right) will be included in the Exclusion process.
2	**Stop**	Stops the series of Stims that are in progress. Note that use of the on-screen blue Stop button will not shut down the System, but use of the yellow Stop button on the front of the Console will.
3	**Progress Bar**	The Progress Bar provides a visual estimate of process progression. It illuminates in different colors to indicate status: Analyzed (blue), Active (white), Stimulating (pink), Unsure (teal), Confirm (light green), and Complete (dark green).
4	**Unsure**	Use the Unsure button to indicate uncertainty about whether an unwanted effect occurred during a Stim. It will prompt the Console to program a Stim with the same electrode combination and intensity again.
5	**Stimulate**	When blue, press the Stimulate button to deliver Stims. This button will also indicate status during stimulations.
6	**Confirm**	Use the Confirm button to indicate that an unwanted effect was observed during a Stim. The Console will use this information to identify the specific electrodes causing the unwanted effect.

To exclude electrodes from Stims:

1. Press the **Exclusion** tab on the Placement, Mapping, or Therapy screen.
2. Press **Stimulate** and observe the patient closely for unwanted effects.

   Note: If needed, stop the delivery of stimulations at any time by pressing the blue **Stop** button on the touchscreen or Handheld Controller.

3. After the Stim is complete, provide feedback to the Console by indicating whether or not an unwanted effect was observed:
   - If you are not sure, select **Unsure** to select the same electrodes again.
   - If the unwanted effect occurred, select **Confirm**.
   - If there were no unwanted effects, do not select either button. It is normal and an expected part of the process to not detect an unwanted effect during a Stim and to move on to the next electrode combination.
4. Repeat steps 2 and 3, following the instructions in the Notification Box, until all electrodes in the array (right or left) have been evaluated, and then press **Complete**.
5. If needed, repeat steps 2 and 3 for the other side (right or left) array, and then press **Complete** again.
6. Press the **Placement**, **Mapping**, or **Therapy** tab; the procedure or session in progress will now continue with the excluded electrodes disabled.

Note: If desired, press **Clear** to undo the completed Exclusion process and turn all electrodes back on. If unwanted effects remain or return, the Exclusion process will need to be repeated.

Note: Excluded electrodes remain disabled for the remainder of the Placement or Therapy session, unless **Clear** is selected.

Notifications

Notifications appear in the notification box above the Stimulate button, and provide additional information about System status.

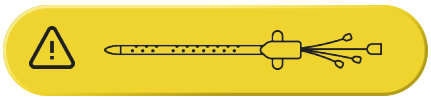
Note: The following notifications only appear on the Mapping and Therapy tabs in Auto mode.

- **Gathering Baseline Data**: Indicates that the Console needs more data from the Airway Sensor before the next Stim can be delivered. Wait while the Airway Sensor continues to gather information about the patient's breathing. If needed, press the blue Stop button to stop the Stim sequence.
- **Pressure Out Of Range**: Indicates that the pressure measured from the Airway Sensor is out of the expected range. Verify that the Airway Sensor is pneumatically connected correctly to the patient's ventilator circuit and verify the patient's ventilator parameters. The notification will go away when the pressure measured on the Airway Sensor returns to the expected range.
- **Baseline Pressure Out Of Range**: Indicates that the baseline pressure measured by the Airway Sensor is out of the expected range. Verify that the Airway Sensor is pneumatically connected correctly to the patient's ventilator circuit and verify the patient's ventilator parameters. The notification will go away when the measured pressure returns to the expected range.
- **Baseline Pressure Inconsistent**: Indicates that the pressure measured on the Airway Sensor is inconsistent. Verify that the Airway Sensor is pneumatically connected correctly to the patient's ventilator circuit and verify the patient's ventilator parameters. The notification will go away when the measured pressure returns to the expected range.
- **Reassessing Baseline Pressure**: Indicates that the baseline pressure measured on the Airway Sensor is inconsistent during a Stim sequence. While this notification is active, the Console will pause Stims to reassess for the baseline pressure data. The notification will go away when the pressure measured from the Airway Sensor stabilizes.
- **Early Breath Detected**: Indicates that the Console detected a breath earlier than expected. The Stim sequence will continue, though stimulation will not be delivered on an early breath. Shortening the Stim Duration, adjusting ventilator settings, and/or delivering Therapy in Manual mode all may help resolve frequent Early Breath Detected notifications.

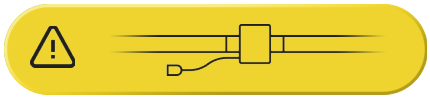
System Warnings

System warnings will appear as a yellow button on the bottom of the screen (in place of the Stimulate button). Press the yellow warning button to view more information.

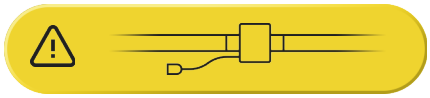
- **Catheter Cable Connection:** Indicates that the Catheter Cable may not be connected to the Catheter, or to the Console. Verify the that the patient's Catheter is securely connected to the Catheter Cable, and that the Catheter Cable is securely connected to the Console.



- **Airway Sensor Cable Connection**: Indicates that the Airway Sensor Cable may not be connected to the Airway Sensor, or to the Console. Verify that the patient's Airway Sensor is securely connected to the Airway Sensor Cable, and that the Airway Sensor Cable is securely connected to the Console.

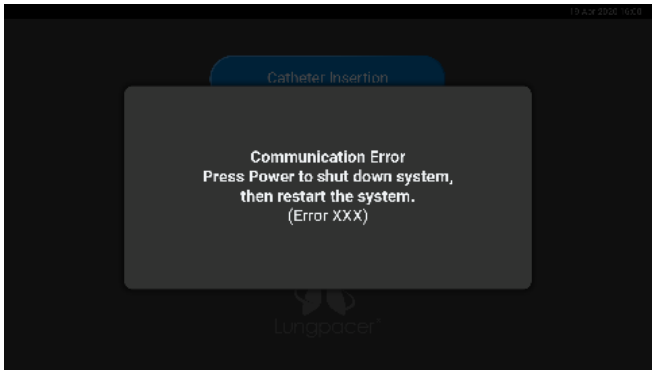


- **Airway Sensor Connection to Patient**: Indicates that the Airway Sensor may not be connected to the patient's ventilator circuit. Verify that the patient's Airway Sensor is properly connected to the patient's ventilator airway circuit. The arrow on the front of the sensor should be oriented toward the patient.



Console Error Messages

Console error messages will appear as pop-ups that cover most of the screen. If these error messages occur, **restart the System by pressing the Power button**, waiting a few seconds, and then pressing the Power button again to turn the System on. If error messages cannot be cleared by restarting the System, make note of the error code at the end of the message, and contact Lungpacer. Example error messages include:



- **Yellow Stop Button Pressed**: Indicates that the yellow Stop button on the front of the Console was pressed, quickly halting all stimulation output.
- **Communication Error**: Indicates that the Console had difficulty communicating internally or with other System components. This message may appear, for example, if there are loose or damaged electrical connections within the Console, between the Console and other System components (such as the Catheter, Airway Sensor, or Handheld Controller), or if other electrical supply or software issues occur.
- **Stimulation Output Error**: Indicates that the Console detected unexpected pulse characteristics such as timing, count, voltage, current, problems with the power supply, or failed an internal integrity check.
- **Logging Error**: Indicates the Console had difficulty writing, exporting, or deleting logs.

System Care and Maintenance

Duration of Use

The AeroPace Neurostimulation Catheter is single-use for a maximum of 30 days, and is provided sterile.

Note: Refer to the AeroPace Neurostimulation Catheter Kit Instructions For Use for information about sterilization processes used on the AeroPace Neurostimulation Catheter and the steps to take in the event of damage to the sterile packaging.

The AeroPace Airway Sensor is single-patient use for a maximum of 30 days.

Cleaning Instructions

WARNING: To reduce the risk of electrical shock, disconnect mains power from the Console before cleaning.

CAUTION:

- Do not disinfect, re-sterilize, or reuse single-patient use or sterile components. Reuse or re-sterilization of sterile components may impair the structural integrity and/or performance of the AeroPace System and may cause injury or infection.
- Follow all cleaning instructions for the System. Improper cleaning of System components may result in infection.

Before use, follow institutional policies regarding cleaning of bedside equipment.

To clean the Airway Sensor, suction the secretions from it, or gently wipe them away using a damp, sterile cloth. Do not rinse the external of Airway Sensor or electrical connector, as this may permanently damage its electronics and cause it to stop functioning.

Wipe down the Catheter Cable, Airway Sensor Cable, Console, and Handheld Controller with a clean, soft, and lint-free cloth. Only the following agents may be used:

- Virox
- Cidex
- Alcohol
- CaviWipes

Disposal

⚠ **CAUTION:** After use, the Catheter, Catheter Kit Components, and/or Airway Sensor may be a potential biohazard. Handle and dispose of them in accordance with accepted medical practice and applicable local, state, and federal laws for biohazardous waste.

Refer to the AeroPace Neurostimulation Catheter Kit Instructions For Use for instructions regarding the removal and disposal of the AeroPace Neurostimulation Catheter.

When the AeroPace Catheter Cable, Airway Sensor Cable, Handheld Controller, or Console are removed from service, adhere to regulations and local guidelines for recycling and disposal of electrical and electronic equipment. To dispose of the Airway Sensor, additionally adhere to local regulations for the disposal of biohazardous waste.

Service Procedures

⚠ **CAUTION:** Do not attempt to open the Console enclosure. Opening the Console may result in electrical shock.

Only qualified personnel may perform AeroPace System service and maintenance procedures. Contact Lungpacer Medical Inc. using the contact details on the back cover of this document for additional information.

System Specifications

Device Classification

The AeroPace System has the following classifications:

- Class III medical device
- Class I Medical Electrical Equipment as per classification in IEC 60601
- IPX1 protected equipment
- Type BF applied parts. The applied parts are the Catheter and the Airway Sensor.

Power Input Rating

Parameter	Specification
Voltage Range	100 to 240 VAC
Power Frequency	50 to 60 Hz
Max Current	1.5 Amps

Note: The AeroPace System is an AC mains-powered system. Connect the Console to a grounded receptacle that supplies AC power of 100 to 240 V, 50 to 60 Hz. A potential-equalization stud for additional grounding is located on the left-hand side of the Console. To use, connect a potential-equalization cable from this stud to an appropriate plug to obtain the additional grounding, if needed.

Operating Conditions

Parameter	Specification
Temperature Range	10 to 40 ˚C (50 to 104 ˚F)
Relative Humidity Range	30 to 90% non-condensing
Altitude	Up to 8000 ft (2438 m) above sea level

Storage Conditions

AeroPace System, excludes AeroPace Neurostimulation Catheter:

Parameter	Specification
Temperature Range	-10 to 60 ˚C (14 to 140 ˚F)
Relative Humidity Range	15% to 90%, non-condensing
Altitude	Up to 8000 ft (2438 m) above sea level

AeroPace Neurostimulation Catheter Kit:

Parameter	Specification
Temperature Range	18 to 28 ˚C (64.5 to 82.4 ˚F)

Transportation Conditions

Parameter	Specification
Temperature Range	-18 to 60 ˚C (-0.4 to 140 ˚F)
Relative Humidity Range	15% to 90%, non-condensing

Output Characteristics

Parameter	Specification
Waveform Type	Charge-balanced biphasic asymmetrical
Pulse Delivery Mode	Constant current stimulation pulses
Pulse Durations	200 µs ± 5% to 300 µs ± 5%
Pulse Repetition Frequencies	15 Hz (default), 20 Hz, 25 Hz, 30 Hz, and 40 Hz options in Therapy for each channel. Typically, 4 Hz in Mapping & Placement. Tolerance: ± 5%
Maximum Voltage	Current regulated 33V maximum
Maximum Current	27.0 mA ± 5% at 300 Ω 27.0 mA ± 5% at 500 Ω 27.0 mA ± 5% at 1000 Ω (typical impedance) 13.0 mA ± 5% at 2000 Ω 6.0 mA ± 5% at 4500 Ω
Net DC Current (nA) at maximum pulse rate	≤ 100 nA

Manufacturer's Declaration – Electromagnetic Compatibility (EMC)

The following accessories were used with the AeroPace Neurostimulation Console in the evaluation of the AeroPace System:

Part Number	Description
000-0055	AeroPace Neurostimulation Console
000-0057	AeroPace Neurostimulation Console Cart
100-0025	Catheter contained within the AeroPace Neurostimulation Catheter Kit (000-0036)
000-0041	AeroPace Airway Sensor
000-0045	AeroPace Airway Sensor Cable
000-0043	AeroPace Catheter Cable
000-0039	AeroPace Handheld Controller

WARNING:

- Only accessories specified or provided by the manufacturer should be used with the AeroPace System. Use of accessories other than those specified may result in increased electromagnetic emissions or decreased electromagnetic immunity.
- Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the AeroPace System. Otherwise, degradation of the performance of the AeroPace System may occur, which may include the system safely entering a state where stimulation is not delivered.
- The AeroPace System should not be used while stacked or placed adjacent to other equipment, as this could result in improper operation of the AeroPace System or other equipment.

Guidance and Manufacturer's Declaration – Electromagnetic Emissions		
The AeroPace System is intended to electrically stimulate the phrenic nerves resulting in activation of the diaphragm while maintaining essential performance, which consists of limiting charge density and stimulation frequency to specified levels. The AeroPace System is intended for use in the electromagnetic environment specified below. The customer or the user of the AeroPace System should assure that it is used in such an environment. Otherwise, degradation of the AeroPace System may occur, which may include the system safely entering a state where stimulation is not delivered.		
Emissions Test	Compliance	Electromagnetic environment - guidance
Radiated RF Emissions CISPR 11	Group 1 Class A	The AeroPace System generates RF energy for its internal function. Interference to nearby electronic equipment is possible.
Conducted Emissions CISPR 11		The AeroPace System is intended for the professional healthcare environment and may not be suitable for connection to the public mains network supplying domestic establishments where CISPR 11 Class B limits are required.[1]
Power Frequency Harmonics IEC 61000-3-2	Class A	The AeroPace System is intended for the professional healthcare environment and may not be suitable for connection to the public mains network supplying domestic establishments.
Voltage Fluctuation/Flicker IEC 61000-3-3	Complies	

Guidance and Manufacturer's Declaration – Electromagnetic Immunity			
The AeroPace System is intended for use in the electromagnetic environment specified below. The customer or the user of the AeroPace System should assure that it is used in such an environment.			
Immunity Test	IEC 60601-1-2 Test level	Compliance level	Electromagnetic environment - guidance
ESD IEC 61000-4-2	±2 kV, ±4 kV, ±8 kV Contact	±2 kV, ±4 kV, ±8 kV Contact	Floors should be wood, concrete, or ceramic tile. If floors are covered with synthetic material, the relative humidity should be at least 30%.
	±2 kV, ±4 kV, ±8 kV, ±15 kV Air	±2 kV, ±4 kV, ±8 kV, ±15 kV Air	
Radiated Immunity IEC 61000-4-3	80 MHz to 1000 MHz 3 V/m Modulation 80%, 1 kHz 1.0 GHz to 2.7 GHz 3 V/m Modulation 80%, 1 kHz	80 MHz to 1000 MHz 3 V/m Modulation 80%, 1 kHz 1.0 GHz to 2.7 GHz 3 V/m Modulation 80%, 1 kHz	Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range.[2]
Proximity field from RF wireless communication equipment	IEC-60601-1-2	See table "Immunity to proximity fields for RF wireless communications equipment"	N/A

1 The EMISSIONS characteristics of this equipment make it suitable for use in industrial areas and hospitals (CISPR 11 class A). If it is used in a residential environment (for which CISPR 11 class B is normally required) this equipment might not offer adequate protection to radio-frequency communication services. The user might need to take mitigation measures, such as relocating or re-orienting the equipment.

2 Field strengths from fixed transmitters, such as base stations for radio (cellular / cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast, and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the AeroPace System is used exceeds the applicable RF compliance levels shown above, the AeroPace System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the AeroPace System.

Guidance and Manufacturer's Declaration – Electromagnetic Immunity			
Proximity field from Common Electromagnetic Emitters	N/A[3]	See table "Immunity to proximity fields for Common Electromagnetic Emitters"	N/A
Electrical Fast Transient / Burst IEC 61000-4-4	AC Mains ±0.5 kV, ±1.0 kV, ±2.0 kV 100 kHz repetition frequency I/O ±0.25 kV, ±0.5 kV, ±1.0 kV 100 kHz repetition frequency	AC Mains ±0.5 kV, ±1.0 kV, ±2.0 kV 100 kHz repetition frequency I/O ±0.25 kV, ±0.5 kV, ±1.0 kV 100 kHz repetition frequency	Mains power quality should be that of a typical commercial or professional healthcare environment.
Surge IEC 61000-4-5	Line to Line (Differential Mode) ±0.5 kV, ±1.0 kV Line to Ground (Common Mode) ±0.5 kV, ±1.0 kV, ±2.0 kV	Line to Line (Differential Mode) ±0.5 kV, ±1.0 kV Line to Ground (Common Mode) ±0.5 kV, ±1.0 kV, ±2.0 kV	Mains power quality should be that of a typical commercial or professional healthcare environment.
Conducted Immunity IEC 61000-4-6	AC Mains, I/O 0.15 MHz to 80 MHz 3 V RMS Modulation: 80% AM, 1 kHz 6.765 MHz to 6.795 MHz 13.553 MHz to 13.567 MHz 26.957 MHz to 27.283 MHz 40.660 MHz to 40.700 MHz 6 V RMS Modulation: 80% AM, 1 kHz	AC Mains, I/O 0.15 MHz to 80 MHz 3 V RMS Modulation: 80% AM, 1 kHz 6.765 MHz to 6.795 MHz 13.553 MHz to 13.567 MHz 26.957 MHz to 27.283 MHz 40.660 MHz to 40.700 MHz 6 V RMS Modulation: 80% AM, 1 kHz	Portable RF communications equipment (including peripherals such as antenna cables and external antennas) should be used no closer than 30 cm (12 inches) to any part of the AeroPace System otherwise degradation of the performance of the AeroPace System may occur, which may include the system safely entering a state where stimulation is not delivered.
Magnetic Immunity IEC 61000-4-8	50 Hz, 60 Hz 30 A/m	50 Hz, 60 Hz 30 A/m	Power frequency fields should be that of a typical commercial or professional healthcare environment.

3 Certain electromagnetic emitters commonly found within the AeroPace System's intended use environment are not adequately addressed by consensus standards. Specific immunity testing was performed for each of these emitters to demonstrate that using the AeroPace System is safe with regard to each identified emitter in the table: "Immunity to proximity fields for Common Electromagnetic Emitters."

Guidance and Manufacturer's Declaration – Electromagnetic Immunity			
Voltage Dips / Interruptions IEC 61000-4-11	Dips 100 VAC 60 Hz, 240 VAC 60 Hz UT = 0%; 0.5 cycle (0°, 45°, 90°, 135°, 180°, 225°, 270°, 315°) UT = 0%; 1 cycle (0°) UT = 70%; 30 cycles (0°) Interruptions 100 VAC 60 Hz, 240 VAC 60 Hz UT = 0%; 300 cycles (0°) UT is the AC Mains voltage prior to application of test level.	Dips 100 VAC 60 Hz, 240 VAC 60 Hz UT = 0%; 0.5 cycle (0°, 45°, 90°, 135°, 180°, 225°, 270°, 315°) UT = 0%; 1 cycle (0°) UT = 70%; 30 cycles (0°) Interruptions 100 VAC 60 Hz, 240 VAC 60 Hz UT = 0%; 300 cycles (0°) UT is the AC Mains voltage prior to application of test level.	Mains power should be that of a typical commercial or professional healthcare environment. If the operator of the AeroPace System requires continuous operation during power mains interruptions, it is recommended that the AeroPace System be powered from an uninterruptable power supply.
RFID Immunity AIM 7351731	RFID Fields ISO/IEC 14223 134.2 kHz, 65 A/m ISO/IEC 14443-3 (Type A) 13.56 MHz, 7.5 A/m ISO/IEC 14443-4 (Type B) 13.56 MHz, 7.5 A/m ISO/IEC 15693 (ISO/IEC 18000-3 (Mode 1)) 13.56 MHz, 5 A/m ISO/IEC 18000-3 (Mode 3) 13.56 MHz, 12 A/m ISO/IEC 18000-7 433.92 MHz, 3 V/m ISO/IEC 18000-63 (Type C) 860 MHz to 960 MHz, 54 V/m ISO/IEC 18000-4 (Mode 1) 2.4 GHz, 54 V/m	RFID Fields ISO/IEC 14223 134.2 kHz, 65 A/m ISO/IEC 14443-3 (Type A) 13.56 MHz, 7.5 A/m ISO/IEC 14443-4 (Type B) 13.56 MHz, 7.5 A/m ISO/IEC 15693 (ISO/IEC 18000-3 (Mode 1)) 13.56 MHz, 5 A/m ISO/IEC 18000-3 (Mode 3) 13.56 MHz, 12 A/m ISO/IEC 18000-7 433.92 MHz, 3 V/m ISO/IEC 18000-63 (Type C) 860 MHz to 960 MHz, 54 V/m ISO/IEC 18000-4 (Mode 1) 2.4 GHz, 54 V/m	Field strengths from fixed RF transmitters, as determined by an electromagnetic site survey, should be less than the compliance level in each frequency range.

Immunity to proximity fields RF wireless communications equipment				
Test Frequency (MHz)	**Band[4] (MHz)**	**Service[5]**	**Modulation**	**Level (V/m)**
385	380 to 390	Tetra 400	Pulse 18 Hz	27
450	430 to 470	GMRS 460, FRS 460	FM 1 kHz sine, ±5 kHz deviation	28
710	704 to 787	LTE Band 13, 17	Pulse 217 Hz, 50% DC	9
745				
780				
810	800 to 960	GSM 800/900, TETRA 800, iDEN 820, CDMA 850, LTE Band 5	Pulse 18 Hz, 50% DC	28
870				
930				
1720	1700 to 1990	GSM 1800; CDMA 1900; GSM 1900; DECT; L TE Band 1, 3, 4, 25; UMTS	Pulse 217 Hz, 50% DC	28
1845				
1970				
2450	2400 to 2570	Bluetooth, WLAN, 802. 11 b/g/n, RFID 2450, LTE Band 7	Pulse 217 Hz, 50% DC	28
5240	5100 to 5800	WLAN 802. 11 a/n	Pulse 217 Hz, 50% DC	9
5500				
5785				

Immunity to proximity fields for Common Electromagnetic Emitters		
Equipment Type / Immunity Test	**Test Frequency**	**Compliance Level**
Diathermy with specific modulation	1.7 MHz to 2.3 MHz	50 V/m
Electrosurgical Cut with protection	1.7 MHz	500 V/m Pulsed
Electrosurgical Coagulate with protection	1.7 MHz	400 V/m Pulsed
X-ray with modulation and protection	30kHz	10 V/m
NFC with multiple modulations	13.56 MHz	81.5 dBuA/m
Wireless Power Transfers (WPT)	Multiple frequencies and modulations	35 dBuA/m
5G Cellular	FR1 Band (with specific modulation)	30 dBm
5G Cellular	FR2 Band (with specific modulation)	15-30 dBm
Metal Detectors	19 different frequencies (mixed modulations)	Up to 400 A/m
Electronic Article Surveillance (EAS)	15 different EAS frequency and modulation combinations	Various uT and A/m power settings

4 Field strengths from fixed transmitters, such as base stations for radio (cellular / cordless) telephones and land mobile radios, amateur radio, AM and FM radio broadcast, and TV broadcast cannot be predicted theoretically with accuracy. To assess the electromagnetic environment due to fixed RF transmitters, an electromagnetic site survey should be considered. If the measured field strength in the location in which the AeroPace System is used exceeds the applicable RF compliance levels shown above, the AeroPace System should be observed to verify normal operation. If abnormal performance is observed, additional measures may be necessary, such as re-orienting or relocating the AeroPace System.

5 For some services, only the uplink frequencies are included.

AeroPace System's Essential Performance Requirements

Per IEC 60601-1, Medical Electrical Equipment Part 1: General requirements for basic safety and essential performance, the AeroPace System's essential performance is defined by the two following requirements:

- The maximum charge density delivered by the system shall be 0.24 mC/cm^2 with an electrode with a gold external surface area.
- The maximum stimulation pulse rate delivered by the System shall be 45 Hz (pulses per second) per side, or less.

The AeroPace System includes an internal subsystem dedicated to constantly monitoring the output characteristics sent from the internal electronics out to the catheter's implanted patient electrodes. These output characteristics are continuously examined to be within the limits of the essential performance requirements listed above. If the internal monitor detects a violation of the essential performance requirements or cannot maintain its operation for any reason, the operator should expect to experience the following:

- Patient stimulation will cease and an error will be displayed on the screen giving context as to why stimulation was stopped.
- In rare circumstances, the Console may cease stimulation and power down without displaying an on-screen error.

Patents

Patents: www.lungpacer.com/patents

Summary of Clinical Trials

RESCUE 3 Study Design

RESCUE 3 was a randomized, controlled, open-label, international multi-center trial using a group sequential design to determine the safety and effectiveness of the AeroPace System plus Standard of Care (SoC) compared with SoC to improve diaphragmatic strength and weaning success in patients on MV. Study subjects were ≥18 years of age and had received MV for ≥96 hours and had failed ≥2 weaning trials. The study was designed to randomize 200 to 400 subjects at a maximum of 80 investigational sites in the United States and Europe. The study duration was 30 days with follow up to Day 32 or study exit.

The primary effectiveness outcome was to demonstrate superiority in the cumulative incidence for successful weaning by Day 30 for subjects randomized to Treatment compared to Control. The primary safety endpoint was to show a consistent risk profile observed for subjects randomized to Treatment compared to Control.

Secondary and observational endpoints compared between the Treatment and Control populations were days on MV, mortality by Day 30, reintubation/reinstatement of MV after successful weaning, change in Maximal Inspiratory Pressure (MIP), and change in Rapid Shallow Breathing Index (RSBI).

The trial was prematurely terminated due to study inclusion and exclusion criteria that slowed enrollment. The study randomized 223 subjects 1:1 blocked by investigational site to the AeroPace System plus SOC (Treatment) or SoC (Control). Forty-eight investigational sites enrolled at least one subject, with 36.3% of subjects randomized in the US and 63.7% in the EU.

One-hundred and nine (109) subjects were randomized to the Treatment group (ITT) and 114 subjects to the Control group (ITT). The modified Intent-to-Treat (mITT) population consisted of 102 subjects and comprised those subjects in the Treatment group with successful placement of the AeroPace Neurostimulation Catheter (defined as entering the vein, at least one phrenic nerve captured, and the diaphragm stimulated). The Per Protocol (PP) population comprised the subset of the mITT population that received ≥50% of the protocol-required number of stimulations and consisted of 90 subjects in the Treatment group. The Control population (ITT) did not receive the AeroPace Neurostimulation Catheter.

Study subjects had been on MV for a mean of 29 days at the time of enrollment. Mean baseline MIP and RSBI were 28.8 cmH_2O and 112.5 breaths/min/L, respectively, indicating a population with diaphragmatic atrophy and low weaning potential (Boles, 2007). The most common reason for subjects being on MV was ARDS/ARF (49.5%), followed by surgery (15.3%), pneumonia independent of COPD, ARDS/ARF or surgery (12.6%), and COPD (11.7%). Fewer than 10% of subjects were on MV for trauma or other reasons. Approximately two-thirds (65%) of the subjects in the Treatment and Control groups had a tracheostomy at the time of enrollment.

The AeroPace System was used to deliver 6 sets of 10 stimulations, twice daily for a total of 120 stimulations/day (stimulation intensity was maximized based on subject comfort) for up to 30 days or until study exit. A Treatment subject could receive a maximum of 3600 stimulations delivered over 30 days. Treatment and Control subjects received SoC for weaning which included one daily protocol-specific weaning trial (maximum of two weaning trials daily).

Effectiveness

The effectiveness of the AeroPace System was evaluated based on data from the 223 randomized RESCUE 3 subjects. Given the unplanned study termination, the study results are reported descriptively.

Successful weaning was numerically superior in the Treatment group compared with the Control group for RESCUE 3 subjects. There were 10.4% (mITT) to 14.1% (PP) more patients in the Treatment group who were successfully weaned compared with the Control group. These results exceeded a pre-specified minimal clinically important difference (MCID) of ≥10%, with a relative risk reduction of remaining on MV by day 30 of up to 37% (RR=.629). RESCUE 3 patients in the Treatment group required, on average, 1.9 (mITT) to 2.4 (PP) fewer days on MV compared with the Control group for up to a 5-fold greater reduction than the pre-specified MCID of 0.5 MV days. Mortality at day 30 was lower by 1.3% for patients in the Treatment group (ITT) compared with the Control group.

Re-intubation rates were 2.4 to 2.6 times lower for patients in the Treatment group (5.6% mITT, 6.1% PP), compared with the Control group (14.5%), for a relative risk reduction for reintubation within 30 days of 60% (RR=0.386, mITT). MIP change from baseline to last available measurement for patients in the Treatment group compared with the Control group was greater by 4.1 cmH_2O (mITT) to 5.1 cmH_2O (PP), a 50% comparatively greater improvement. RSBI was numerically improved from baseline for patients in the Treatment group (mITT: -35.0 breaths/min/L, p=0.252; PP: -37.0 breaths/min/L, p=0.209) compared to the Control group (-19.9 breaths/min/L).

Patients in the Treatment group had numerically fewer tracheostomies over 30 days (mITT: 12.8%; PP: 11.4%) compared with the Control group (18.8%). Patients in the Treatment group also required reduced ventilator requirements from Day 1 to last available measurement for pressure support (mITT: -1.9 ±5.0 cmH_2O, PP: -2.0 ±4.9 cmH_2O) compared with the Control group (-0.1 ±4.5 cmH_2O) and for fraction of inspired oxygen (mITT: -2.7% ±8.6; PP: -3.0% ±8.7), compared with the Control group (0.1% ±10.9).

The RESCUE 3 effectiveness outcomes are summarized in the table below.

Effectiveness Endpoint	Analysis Population	Treatment (95% CI) [min, med, max]	Control (95% CI) [min, med, max]	Treatment Minus Control (95%CI)
Successful Weaning (%)	mITT	72.4% (62.1, 80.3)	62.0% (52.2, 70.4)	10.4%
	PP	76.1% (65.4, 83.9)	62.0% (52.2, 70.4)	14.1%
Days on MV (Days)	mITT	15.5 ± 10.2 [0,0, 12.0, 29.0]	17.3 ± 10.9 [1.0, 18.0, 29.0]	-1.9 (-4.8, 1.0)
	PP	14.9 ± 9.9 [0,0, 12.5, 29.0]	17.3 ± 10.9 [1.0, 18.0, 29.0]	-2.43 (-5.3, 0.5)
Mortality (%)	ITT	9.2% (3.8, 14.6)	10.5% (4.9, 16.2)	-1.3%
Reintubation (%)	mITT	5.6% (2.7, 11.0)	14.5% (6.2, 22.8)	-8.9% (-18.7, 1.0)
	PP	6.1% (3.0, 11.8)	14.5% (6.2, 22.8)	-8.4% (-18.5, 1.7)
MIP (cm H_2O, absolute)	mITT	13.9 ± 19.3 [-32.7, 12.8, 81.9]	9.8 ± 15.2 [-32.5, 7.7, 48.4]	4.1 (-0.6, 8.8)
	PP	14.9 ± 19.9 [-32.7, 13.7, 81.9]	9.8 ± 15.2 [-32.5, 7.7, 48.4]	5.1 (0.1, 10.1)
RSBI (breaths/min/L)	mITT	-35.0 ± 107.9 [-819.9, -12.2, 258.6]	-19.8 ± 78.2 [-611.7, -8.6, 225.0]	-15.1 (-41.1, 10.8)
	PP	-37.0 ± 106.4 [-819.9, -12.4, 71.4]	-19.8 ± 78.2 [-611.7, -8.6, 225.0]	-17.2 (-44.1, 9.7)

CI = Confidence Interval; ITT = Intent-to-Treat; mITT = Modified Intent-to-Treat; MIP = Maximal Inspiratory Pressure; MV = Mechanical Ventilation; RSBI = Rapid Shallow Breathing Index Note: All confidence intervals are nominal without adjustment of multiplicity [1] Two-sided 95% confidence interval

In summary, while statistical success criteria were not pre-specified for the 223 randomized subject population, pre-specified MCIDs between the Treatment group compared with the Control group were exceeded for the primary endpoint of successful weaning and for the secondary endpoint of days on MV indicating clinically significant outcomes, which along with superior outcomes across multiple study endpoints established evidence of device effectiveness.

Safety

Adverse events (AEs) and serious adverse events (SAEs) were collected through Day 30 unless the patient was withdrawn from the study or died. Patients in the Treatment group with an unsuccessful Catheter placement were followed for 48 hours for post-procedural complications and then exited from the study. Patients who did not wean by Day 30, had their AeroPace Neurostimulation Catheter removed on Day 30 and were then followed for 48 hours (Day 32) for safety events. AEs and SAEs were categorized by MedDRA System Organ Class (SOC) and lower-level term (LLT).

There were 189 AEs in 74 Treatment subjects (67.9%) and 152 AEs in 60 Control subjects (52.6%). Among all AEs, 70 events in 39 Treatment subjects (35.8%) and 46 events in 27 Control subjects (23.7%) were SAEs. The number and types of AEs reported were consistent with an expected safety profile of critically ill, mechanically ventilated patients. The higher incidence of catheter-related events in Treatment subjects reflect higher (100%) catheter usage compared with Control subjects (typically 50%-80%, Climo, 2003).

AE and SAEs, by SOC, that occurred in >10% of Treatment group subjects are shown in the table below. There were no AEs or SAEs of ventilator dyssynchrony with stimulation or reports of diaphragm injury. The Catheter was used for fluid delivery in 63.8% (65/102) of mITT Treatment subjects and there were no AEs reported related to use of the Catheter for fluid delivery.

AEs and SAEs in Treatment Group (ITT) with ≥10% Incidence

Body System Organ Class	Adverse Events				Serious Adverse Events*			
	Treatment N=109		Control N=114		Treatment N=109		Control N=114	
	# of events	# (%) of Subjects	# of events	# (%) of Subjects	# of events	# (%) of subjects	# of events	# (%) of subjects
Infections	44	34 (31.2%)	37	27 (23.7%)	22	19 (17.4%)	16	12 (10.5%)
Respiratory, thoracic and mediastinal disorders	33	27 (24.8%)	32	24 (21.1%)	15	14 (12.8%)	16	13 (11.4%)
Cardiac disorders	21	17 (15.6%)	15	11 (9.6%)	13	12 (11.0%)	2	2 (1.8%)
Vascular disorders	17	15 (13.8%)	8	8 (7.0%)	1	1 (0.9%)	2	2 (1.8%)
Gastrointestinal disorders	16	11 (10.1%)	11	9 (7.9%)	6	4 (3.7%)	3	3 (2.6%)

*SAE relationship and seriousness were adjudicated by the study Clinical Events Committee. AE relationship and seriousness were determined by the investigator.

AEs and SAEs determined to be possibly, probably, or definitely related to the study device and/or procedure are shown

by SOC in the table below. There were no unanticipated adverse device events.

The overall incidence of device- or procedure-related AEs in the Treatment group was 21.1% (36 events in 23 subjects). The most frequent device- or procedure-related AEs by SOC were infections (9.2%), cardiac disorders (6.4%), and vascular disorders (3.7%). Other less frequent related AEs were procedural or catheter placement complications. AEs for infection were mostly related to the device rather than the procedure and were associated with catheter insertion and use. AEs for cardiac disorders were mainly due to inadvertent cardiac stimulation associated with the device for transvenous neurostimulation. Vascular AEs were mostly related to the device and were associated with catheter placement (hemothorax/pneumothorax).

The overall incidence of deviceor procedure-related SAEs was 9.6% (12 events in 11 subjects). The most frequently reported related SAEs by SOC were infections (6.1%) and cardiac disorders (2.6%). Infection and cardiac disorder device- or procedure-related SAEs were predominantly related to the device rather than the procedure. Cardiac SAEs were associated with inadvertent cardiac stimulation due to transvenous stimulation during electrode mapping (1.8%) or were related to catheter misplacement (0.9%). These AEs were temporary, were resolved by stopping stimulation with no further sequelae, and did not occur in subsequent sessions. Acute coronary syndrome in one (1) subject who died was possibly related to the procedure due to possible undetected tension pneumothorax. There was one vascular SAE of hypovolemic shock in one (1) subject who died that was possibly related to the device due to hemothorax / pneumohemothorax.

Deaths occurred in 9.2% (10/109) of ITT subjects in the Treatment group and 10.5% (12/114) of ITT subjects in the Control group due to cardiac/cardiopulmonary shock, organ failure, respiratory failure, or ARDS/pneumonia. Mortality was at the lower end of the expected range of 10% to 30% for this critically ill population.

Discomfort and pain assessment was conducted using a 10-point visual analogue pain rating scale before and after each therapy session. The mean pain scale rating before and after all therapy sessions for mITT Treatment subjects was negligible with an increase of 0.2 points (2% of the 10-point scale). The percentage of sessions in which subjects perceived any pain after therapy was approximately 8% (8/102) indicating therapy was well tolerated even with stimulation delivered at maximum intensity in 83% (85/102) of subjects.

Procedure/Device-Related AEs and SAEs in Treatment Subjects by SOC (ITT)

Body System Organ Class	Procedure or Device-Related Adverse Events		Procedure or Device-Related Serious Adverse Events	
	# of events	# (%) of subjects	# of events	# (%) of Subjects
Infections and infestations	11	10 (9.2%)	7	7 (6.1%)
Cardiac disorders	10	7 (6.4%)	4	3 (2.6%)
Injury, poisoning and procedural complications	6	3 (2.8%)	0	0
Vascular disorders	4	4 (3.7%)	1	1 (0.9%)
General disorders and administration site conditions	3	3 (2.8%)	0	0
Blood and lymphatic system disorders	1	1 (0.9%)	0	0
Surgical and medical procedures	1	1 (0.9%)	0	0
Total	**36**	**23 (21.1%)**	**12**	**11 (9.6%)**

*SAE relationship and seriousness adjudicated by the Clinical Events Committee. AE relationship and seriousness determined by the investigator.

In summary, safety events in the RESCUE 3 trial were as expected for a patient population on mechanical ventilation. Safety events related to the AeroPace System, or its procedures, were those expected for a CVC (Rai, 2023; Smit, 2018) delivering transvenous electrical neurostimulation. Transvenous neurostimulation may cause inadvertent cardiac stimulation during electrode mapping or therapy. These expected cardiac events were temporary, occurred at a low incidence (2.6%), and were resolved without sequelae.

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Glossary of Symbols

Symbol	Meaning	Symbol	Meaning
	Caution		Use by
	Warning		Do not re-use
	Consult instructions for use		Sterilized using ethylene oxide
	Keep dry		Do not re-sterilize
	Keep away from sunlight		Mass
	Do not use if package is damaged		Fuse
Rx Only	Prescription only		Waste Electrical and Electronic Equipment
	Type BF applied part		Equipotentiality
	Manufacturer	IPX1	Protected against vertically falling water drops
	Date of manufacture		Temperature limit
REF	Catalogue number	MD	Medical device
SN	Serial number		Open here
LOT	Batch code		

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