DEVICE AND METHOD FOR MANIPULATING MINUTE VENTILATION

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ABSTRACT
A stimulation device is provided that stimulates breathing to manipulate blood gas concentrations such as SaO₂ or PCO₂ and thereby treat underlying causes of breathing disorders and heart failure progression. A programmable device is provided for setting diaphragm stimulation waveforms that adjust minute ventilation about a predetermined baseline value. Normal breathing of the subject is observed to establish a baseline reference minute ventilation, and the device is programmed to produce stimulation waveforms that may provide either a decrease or an increase in the patient's minute ventilation. The minute ventilation of the subject may be decreased or increased from the baseline level by decreasing or increasing a parameter that changes minute ventilators.
<table>
<thead>
<tr>
<th>Respiratory Rate (RR)</th>
<th>RR_d</th>
<th>RR_n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease X%</td>
<td>(1-X/100)*Observed</td>
<td>Observed</td>
</tr>
<tr>
<td>Increase Y%</td>
<td>(1+Y/100)*Observed</td>
<td></td>
</tr>
</tbody>
</table>

**FIG. 2**

<table>
<thead>
<tr>
<th>Tidal Volume</th>
<th>Normal</th>
<th>Normal</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Rate (RR)</td>
<td>RR_d</td>
<td>RR_n</td>
<td>RR_j</td>
</tr>
<tr>
<td>Inspiration Duration</td>
<td>ID_d</td>
<td>ID_n</td>
<td>ID_j</td>
</tr>
</tbody>
</table>

**FIG. 3**
Attach Flow Sensor

Observe Normal Tidal Volume and Normal Rate

Measure and Store EMG, Tidal Volume, Inspiration Duration, and Respiratory Rate

Determine Inspiration Duration ID$_n$

Observe Normal Tidal Volume and Decreased Rate

Measure and Store EMG, Tidal Volume, Inspiration Duration, and Respiratory Rate

Determine Inspiration Duration ID$_d$

Observe Normal Tidal Volume and Increased Rate

Measure and Store EMG, Tidal Volume, Inspiration Duration, and Respiratory Rate

Determine Inspiration Duration ID$_i$

Done

FIG. 4
### FIG. 5

<table>
<thead>
<tr>
<th>Tidal Volume (10-30%)</th>
<th>Respiratory Rate (30-50%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mis</td>
<td></td>
</tr>
</tbody>
</table>

### Minute Ventilation Changes

<table>
<thead>
<tr>
<th>Respiratory Rate</th>
<th>Inspiration Duration</th>
<th>Tidal Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR_d</td>
<td>ID_d</td>
<td>Decreased</td>
</tr>
<tr>
<td>RR_n</td>
<td>ID_n</td>
<td></td>
</tr>
<tr>
<td>RR_i</td>
<td>ID_i</td>
<td></td>
</tr>
</tbody>
</table>

**FIG. 6**
Set Normal Tidal Volume Target

Set Inspiration Duration = IDₙ

Set Stimulation Waveforms for Normal Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

Yes

Store Stimulation Parameters for Normal Tidal Volume and Normal Respiratory Rate

No

Adjust Stimulation Waveform

Done

FIG._7
Set Normal Tidal Volume Target

Set Inspiration Duration = ID_d

Set Stimulation Waveforms for Normal Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

Adjust Stimulation Waveform

Yes

Store Stimulation Parameters for Normal Tidal Volume and Decreased Respiratory Rate

Done

FIG._8
Set Normal Tidal Volume Target

Set Inspiration Duration = IDᵢ

Set Stimulation Waveforms for Normal Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

Yes

Store Stimulation Parameters for Normal Tidal Volume and Increased Respiratory Rate

No

Adjust Stimulation Waveform

Done

FIG._9
Set Decreased Tidal Volume Target

Set Inspiration Duration = ID_n

Set Stimulation Waveforms for Decreased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

Adjust Stimulation Waveform

Store Stimulation Parameters for Decreased Tidal Volume and Normal Respiratory Rate

Done

FIG. 10
Set Decreased Tidal Volume Target

Set Inspiration Duration = ID_d

Set Stimulation Waveforms for Decreased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

No: Adjust Stimulation Waveform

Yes: Store Stimulation Parameters for Decreased Tidal Volume and Decreased Respiratory Rate

Done

FIG. 11
Set Decreased Tidal Volume Target

Set Inspiration Duration = IDᵢ

Set Stimulation Waveforms for Decreased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target? - No

Adjust Stimulation Waveform

Does Tidal Volume Meet Target? - Yes

Store Stimulation Parameters for Decreased Tidal Volume and Increased Respiratory Rate

Done

FIG. 12
Set Increased Tidal Volume Target

Set Inspiration Duration = ID

Set Stimulation Waveforms for Increased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

- Yes: Store Stimulation Parameters for Increased Tidal Volume and Normal Respiratory Rate
- No: Adjust Stimulation Waveform

Done
Set Increased Tidal Volume Target

Set Inspiration Duration = ID_d

Set Stimulation Waveforms for Increased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

No → Adjust Stimulation Waveform

Yes → Store Stimulation Parameters for Increased Tidal Volume and Decreased Respiratory Rate

Done

FIG. 14
Set Increased Tidal Volume Target

Set Inspiration Duration = ID

Set Stimulation Waveforms for Increased Tidal Volume

Deliver Stimulation Waveform

Measure Response to Stimulation

Does Tidal Volume Meet Target?

Adjust Stimulation Waveform

Yes

Store Stimulation Parameters for increased Tidal Volume and increased Respiratory Rate

Done

FIG.15
DEVICE AND METHOD FOR MANIPULATING MINUTE VENTILATION

RELATED APPLICATION DATA


FIELD OF THE INVENTION

[0002] The present invention relates to devices, systems, and methods useful for providing ventilation through stimulation of the diaphragm.

BACKGROUND OF THE INVENTION

[0003] The human body’s ability to maintain homeostasis is due in part due to respiratory functions controlled by the brain and associated feedback systems. In maintaining homeostasis, respiratory functions typically alter both blood oxygen saturation and carbon dioxide partial pressures.

[0004] Certain pathological conditions such as circulation delay in heart failure patients may lead to instability in the respiratory feedback systems. Circulatory delay is believed to cause phase shift or time delay in the inherent blood gas sensing feedback loop. One manifestation of this is resulting breathing disorders including periodic breathing, Cheyne-Stokes, and apnea (predominantly central sleep apnea (CSA)). Cheyne-Stokes respiration is believed to occur in part because of this circulatory delay and perceived drop in SaO2 levels. Central apnea, and, in some cases obstructive apnea, is believed to occur in part due to a drop in partial pressure of CO2 following a Cheyne-Stokes hyperventilation pattern. Other conditions such as congestive heart failure (CHF) may be able to derive a benefit by an increase in the partial pressure of O2 above which is normally maintained.

[0005] Mechanical ventilators have been used to take over breathing to ensure adequate oxygen levels in patients who cannot sufficiently breathe on their own or who stop breathing at night during apnea events. Mechanical ventilators control the inflow and egress of respiratory gasses by controlling combinations of flow, pressure and/or volume. The ventilator delivers an inspiration via positive pressure delivered into the trachea and lungs and can control exhalation by manipulating pressure and flow.

[0006] Diaphragm stimulation has been used to create respiration in patients who cannot breathe on their own and has been suggested to stimulate breathing when apnea occurs. Diaphragmatic stimulation has generally been used to control inspiration via contraction of the diaphragm muscle which creates negative intra-thoracic pressure resulting in inspiration. Exhalation has generally been a passive process driven by lung and thoracic compliance.

[0007] The ventilators and proposed diaphragm stimulation have not addressed the causes of breathing disorders, but rather have been limited to supplementing breathing when breathing is insufficient or not present.

BRIEF SUMMARY OF THE INVENTION

[0008] The present invention provides an implantable device for delivering electrical stimulation waveforms to the diaphragm through one or more electrodes. In particular, one aspect of the invention provides stimulation waveforms that are directed to manipulation of patient blood gases, e.g., SaO2 and PCO2. In order to achieve manipulation of blood gas concentration, in one embodiment minute ventilation is increased or decreased with respect to a baseline minute ventilation. This may be done by manipulation of one or more parameters affecting minute ventilation. Some of the parameters may include, for example, tidal volume, respiration rate, flow morphology, flow rate, inspiration duration, slope of the inspiration curve, and diaphragm-created or intrathoracic pressure gradients. The implantable device may be programmed by a programmer that is coupled to a flow sensor that measures the natural respiration and stimulation respiration of a subject. Normal breathing of a patient is observed to establish a baseline reference minute ventilation, and the device is programmed to produce stimulation waveforms that may provide either a decrease or an increase in the patients minute ventilation.

[0009] In one embodiment of the invention the reference minute ventilation of a patient is obtained by observing normal breathing of a patient in an awake state, and increased and decreased minute ventilation are obtained by interacting with the patient.

[0010] In another embodiment the reference minute ventilation of a patient is obtained by observing the patient in the sleeping state, and increased and decreased minute ventilation are obtained by applying a predetermined multiplier.

[0011] In yet another embodiment the minute ventilation is decreased from the reference level by decreasing one or more of the following parameters: respiratory rate, inspiration duration, and tidal volume.

[0012] In still another embodiment the minute ventilation is increased from the reference level by increasing one or more of the following parameters: respiratory rate, inspiration duration, and tidal volume.

[0013] In a further embodiment an electrical stimulation waveform is provided for creating an enhanced negative intrapleural pressure during exhalation.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] FIG. 1 shows a diagram of a diaphragm stimulator device in accordance with the present invention.

[0015] FIG. 2 shows a parameter table for selected respiratory rates in accordance with the invention.

[0016] FIG. 3 shows a parameter table for measured inspiration duration in accordance with the invention.

[0017] FIG. 4 shows a flow diagram for establishing a baseline respiratory reference in accordance with the invention.

[0018] FIG. 5 shows a parameter table for diaphragm stimulation parameters in accordance with the invention.

[0019] FIG. 6 shows a parameter table of the respiratory changes associated with stimulation combinations in accordance with the invention.

[0020] FIG. 7 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and a normal respiratory rate in accordance with the invention.

[0021] FIG. 8 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and a decreased respiratory rate in accordance with the invention.

[0022] FIG. 9 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and an increased respiratory rate in accordance with the invention.
FIG. 10 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and a normal respiratory rate in accordance with the invention.

FIG. 11 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and a normal respiratory rate in accordance with the invention.

FIG. 12 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and an increased respiratory rate in accordance with the invention.

FIG. 13 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and a normal respiratory rate in accordance with the invention.

FIG. 14 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and a decreased respiratory rate in accordance with the invention.

FIG. 15 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and an increased respiratory rate in accordance with the invention.

FIG. 16 shows a stimulation waveform for providing exhalation bias in accordance with the invention.

DETAILED DESCRIPTION OF THE INVENTION

FIG. 1 shows a diagram of a system 100 for diaphragm stimulation in accordance with the invention. A subject 105 is implanted with a programmable stimulation device 130 that is coupled to one or more electrodes 125 in contact with the diaphragm 120. The one or more electrodes 125 may include both sensing and stimulation electrodes. A flow measuring device 110 (e.g., a pneumotachometer) is used to measure the respiratory flow characteristics (e.g., tidal volume, inspiration duration, and respiratory rate) of the subject 105.

A programmer 140 is coupled to the flow measuring device 110. The programmer 140 is also coupled to the implanted programmable stimulating device 130 by a telemetry wand 135. An optional sensor 115 may also be coupled to the subject 105 and to the programmer for collecting respiratory and/or blood gas composition data (e.g., pulse oximetry or exhaled gas composition).

The system 100 may be used to determine a minute ventilation baseline reference value for the subject and the device 130 may be programmed to provide a waveform stimulus to adjust the minute ventilation of the subject about the baseline reference value. Minute ventilation is the tidal volume x respiratory rate for a minute of time. Minute ventilation may be determined by an ensuing tidal volume over time or an instantaneous value. The minute ventilation of the subject generally increases or decreases with increase or decrease in energy (e.g., frequency, current, pulse width, or amplitude) applied to the diaphragm. The energy applied by the device 130 may be adjusted by selection of the amplitude, frequency, pulse width, and duration of the series of pulses or stimulus waveform applied by the device 130.

The device may be programmed to produce stimulation waveforms that vary the combination of respiratory rate and tidal volume which result in an increase or decrease of minute ventilation from a reference level. Increasing minute ventilation generally increases the partial pressure of O₂ compared to a reference minute ventilation. Decreasing minute ventilation generally increases the partial pressure of CO₂ compared to a reference minute ventilation. Accordingly, the invention provides a method and device that manipulates blood gas concentration.

The system shown in diagram 100 may be used to observe the natural normal, or intrinsic respiration of a subject in either the waking state or the sleeping state. When the flow measuring device 110 is a pneumotachometer, the subject will more likely be in the waking state.

The device 130 may be programmed to provide stimulation assistance that is correlated with normal respiration (RRₙ), decreased respiration rate (RRₘ), or increased respiration rate (RRᵢ). FIG. 2 shows a parameter table for selecting respiratory rates in accordance with an embodiment of the present invention. The value for RRₙ is selected as a fixed percentage (100-X) of the observed normal respiratory rate of the subject. Similarly, the value for RRₘ is selected as a fixed percentage (100+Y) of the observed normal respiratory rate of the subject.

Typically, inspiration duration is not constant and will vary inversely with the respiration rate. Thus, a decreased inspiration duration IDₘ is associated with an increased respiratory rate RRₘ and an increased inspiration duration IDᵢ is associated with a decreased respiratory rate RRᵢ. In order to establish the duration of the stimulus waveform for a constant tidal volume, the subject's inspiration duration is measured while breathing at the selected breathing rates. In this example, the target tidal volume is the same as the observed normal tidal volume value.

For stimulation therapy that is to be delivered while a patient is sleeping, the most accurate baseline respiratory rate and tidal volume are those that are observed while the subject is asleep. However, since monitoring of a sleeping subject may not provide the required respiratory rates at the normal tidal volume, a waking subject may be coached to provide the required tidal volume and respiratory rate combinations so that the associated inspiration duration can be measured. A clinician will typically allow a period of time for the subject to be relaxed. Alternatively, hypnosis or meditative techniques may be used to place the subject in a suitable state. In order to obtain defined parameter values an average over two or more inspiration/exhalation cycles may be taken.

FIG. 4 shows a flow diagram for establishing a baseline respiratory reference for a subject in accordance with a method embodiment of the present invention. In step 405 a flow sensor (e.g., a pneumotachometer) is attached to the subject. In step 410 the normal tidal volume and normal inspiration rate are observed. In step 415, when the subject is in a satisfactory state, the electromyogram (EMG) of the diaphragm, tidal volume, and inspiration duration are measured and recorded. In step 420 the normal inspiration duration IDₙ is determined. The value for IDₙ may be an average of selected observed values (e.g., a moving average).

In step 425 a decreased inspiration rate at the normal tidal volume is observed. In step 430 the electromyogram (EMG) of the diaphragm, tidal volume, and inspiration duration are measured and recorded. The subject may be breathing spontaneously or may be coached. In step 435 the decreased inspiration duration IDᵢ is determined. The value for IDᵢ may be an average of selected observed values (e.g., a moving average).

In step 440 an increased inspiration rate at the normal tidal volume is observed. In step 445 the electromyogram (EMG) of the diaphragm, tidal volume, and inspiration duration are measured and recorded. The subject may be breathing spontaneously or may be coached. In step 450 the increased
inspiration duration ID, is determined. The value for ID, may be an average of selected observed values (e.g., a moving average). At step 455 the baseline reference determination is complete. While the ID, and ID, may be measured as noted, they also may be calculated based on the ID, for example, as a percentage change from the ID,.

[0041] FIG. 5 shows a parameter selection table for diaphragm stimulation parameters in accordance with an embodiment of the present invention. Diaphragm stimulation may be used to adjust minute ventilation by varying the tidal volume and/or respiratory rate. The preferred range for the change in tidal volume from normal is 10-30% of normal and the preferred range for the change in respiratory rate from normal is 30-50%.

[0042] When applying stimulus waveforms between cycles in a subject's spontaneous breathing pattern, the inspiration duration must be correlated with the subject's respiratory rate. Thus, although the tidal volume may be adjusted through adjustments in inspiration duration, it is preferable to adjust the tidal volume by adjusting the frequency and amplitude of the stimulus waveform.

[0043] FIG. 6 shows a parameter table of the minute ventilation changes associated with stimulation combinations in accordance with an embodiment of the present invention. The table in FIG. 6 is a 3x3 matrix of minute ventilation that is the product of respiratory rate (at a given inspiration duration) and tidal volume. The up and down arrows in the matrix of the table in FIG. 6 correspond to a respective increase or decrease in minute ventilation in relation to the minute ventilation for normal tidal volume and RR/ID,.. For example, the combination of RR/ID, and decreased tidal volume result in a decrease in minute ventilation, and the combination of RR/ID, and increased tidal volume produce an increase in minute ventilation. These results are consistent regardless of the percent change selected for tidal volume and respiratory rate within the preferred ranges shown in FIG. 5.

[0044] It should be noted that the combination of RR/ID, and decreased tidal volume may produce either an increase or decrease in minute ventilation, depending upon the values selected for percent change in tidal volume and respiratory rate. The discrete values in the table of FIG. 6 may be used to provide limits for continuously variable parameters. Continuous parameter functions may be obtained by interpolation of discrete values.

[0045] FIG. 7 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and a normal respiratory rate in accordance with a method embodiment of the present invention. In step 705 the observed normal tidal volume is selected as a target. In step 710 the waveform inspiration duration is set to the ID, associated with the normal respiratory rate.

[0046] In step 715 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp value variations (i.e., increases in amplitude and/or frequency during a stimulation burst or series of pulses. These values are selected to produce the observed normal tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data. A discussion of diaphragm mapping and stimulus waveforms may be found in application Ser. No. 10/686,891, "BREATHING DISORDER DETECTION AND THERAPY DELIVERY DEVICE AND METHOD", by Tehrani et al., filed Oct. 15, 2003, and incorporated herein by reference, and in related U.S. patent application entitled "SYSTEM AND METHOD FOR MAPPING DIAPHRAGM ELECTRODE SITES" filed on even date herewith.

[0047] In step 720 the stimulation waveform is delivered to the diaphragm. In step 725 the response to the stimulation waveform is measured. In step 730 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 705. If the criterion is not met step 735 is executed. In step 735 the stimulation waveform is adjusted. If the criterion is met in step 730, step 740 is executed. In step 740 the waveform parameters are stored for normal tidal volume at normal respiratory rate. In step 745 the stimulation waveform parameters are established.

[0048] FIG. 8 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and a decreased respiratory rate in accordance with a method embodiment of the present invention. In step 805 the observed normal tidal volume is selected as a target. In step 810 the waveform inspiration duration is set to the ID, associated with the decreased respiratory rate for example, as determined herein with reference to FIG. 2 or 3.

[0049] In step 815 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the observed normal tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0050] In step 820 the stimulation waveform is delivered to the diaphragm. In step 825 the response to the stimulation waveform is measured. In step 830 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 805. If the criterion is not met step 835 is executed. In step 835 the stimulation waveform is adjusted. If the criterion is met in step 830, step 840 is executed. In step 840 the waveform parameters are stored for normal tidal volume at decreased respiratory rate. In step 845 the stimulation waveform parameters are established.

[0051] FIG. 9 shows a flow diagram for establishing stimulation waveforms with a normal tidal volume and an increased respiratory rate in accordance with a method embodiment of the present invention. In step 905 the observed normal tidal volume is selected as a target. In step 910 the waveform inspiration duration is set to the ID, associated with the increased respiratory rate.

[0052] In step 915 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the observed normal tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0053] In step 920 the stimulation waveform is delivered to the diaphragm. In step 925 the response to the stimulation waveform is measured. In step 930 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 905. If the criterion is not met step 935 is executed. In step 935 the stimulation waveform is adjusted. If the criterion is met in step 930, step 940 is executed. In step 940 the waveform parameters are
stored for normal tidal volume at increased respiratory rate. In step 945 the stimulation waveform parameters are established.

[0054] FIG. 10 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and a normal respiratory rate in accordance with a method embodiment of the present invention. In step 1005 the observed decreased tidal volume is selected as a target. In step 1010 the waveform inspiration duration is set to the IDₜ associated with the normal respiratory rate.

[0055] In step 1015 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected decreased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0056] In step 1020 the stimulation waveform is delivered to the diaphragm. In step 1025 the response to the stimulation waveform is measured. In step 1030 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1005. If the criterion is not met step 1035 is executed. In step 1035 the stimulation waveform is adjusted. If the criterion is met in step 1030, step 1040 is executed. In step 1040 the waveform parameters are stored for decreased tidal volume at normal respiratory rate. In step 1045 the stimulation waveform parameters are established.

[0057] FIG. 11 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and a decreased respiratory rate in accordance with a method embodiment of the present invention. In step 1105 the observed decreased tidal volume is selected as a target. In step 1110 the waveform inspiration duration is set to the IDₜ associated with the decreased respiratory rate.

[0058] In step 1115 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected decreased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0059] In step 1120 the stimulation waveform is delivered to the diaphragm. In step 1125 the response to the stimulation waveform is measured. In step 1130 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1105. If the criterion is not met step 1135 is executed. In step 1135 the stimulation waveform is adjusted. If the criterion is met in step 1130, step 1140 is executed. In step 1140 the waveform parameters are stored for decreased tidal volume at decreased respiratory rate. In step 1145 the stimulation waveform parameters are established.

[0060] FIG. 12 shows a flow diagram for establishing stimulation waveforms with a decreased tidal volume and an increased respiratory rate in accordance with a method embodiment of the present invention. In step 1205 the observed decreased tidal volume is selected as a target. In step 1210 the waveform inspiration duration is set to the IDₜ associated with the increased respiratory rate.

[0061] In step 1215 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected decreased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0062] In step 1220 the stimulation waveform is delivered to the diaphragm. In step 1225 the response to the stimulation waveform is measured. In step 1230 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1205. If the criterion is not met step 1235 is executed. In step 1235 the stimulation waveform is adjusted. If the criterion is met in step 1230, step 1240 is executed. In step 1240 the waveform parameters are stored for decreased tidal volume at increased respiratory rate. In step 1245 the stimulation waveform parameters are established.

[0063] FIG. 13 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and a normal respiratory rate in accordance with a method embodiment of the present invention. In step 1305 the selected increased tidal volume is selected as a target. In step 1310 the waveform inspiration duration is set to the IDₜ associated with the normal respiratory rate.

[0064] In step 1315 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected increased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0065] In step 1320 the stimulation waveform is delivered to the diaphragm. In step 1325 the response to the stimulation waveform is measured. In step 1330 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1305. If the criterion is not met step 1335 is executed. In step 1335 the stimulation waveform is adjusted. If the criterion is met in step 1330, step 1340 is executed. In step 1340 the waveform parameters are stored for increased tidal volume at normal respiratory rate. In step 1345 the stimulation waveform parameters are established.

[0066] FIG. 14 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and a decreased respiratory rate in accordance with a method embodiment of the present invention. In step 1405 the selected increased tidal volume is selected as a target. In step 1410 the waveform inspiration duration is set to the IDₜ associated with the decreased respiratory rate.

[0067] In step 1415 the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected increased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

[0068] In step 1420 the stimulation waveform is delivered to the diaphragm. In step 1425 the response to the stimulation waveform is measured. In step 1430 a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1405. If the criterion is not met step 1435 is executed. In step 1435 the stimulation waveform is adjusted. If the criterion is met in step 1430, step 1440 is executed. In step 1440 the waveform parameters are stored for increased tidal volume at decreased respiratory rate. In step 1445 the stimulation waveform parameters are established.
FIG. 15 shows a flow diagram for establishing stimulation waveforms with an increased tidal volume and an increased respiratory rate in accordance with a method embodiment of the present invention. In step 1505, the selected increased tidal value is selected as a target. In step 1510, the waveform inspiration duration is set to the ID associated with the increased respiratory rate.

In step 1515, the stimulation waveforms are given initial amplitude and frequency values, and initial amplitude and frequency ramp values. These values are selected to produce the selected increased tidal volume. The values may be selected on the basis of information specific to the subject such as previously observed mapping data.

In step 1520, the stimulation waveform is delivered to the diaphragm. In step 1525, the response to the stimulation waveform is measured. In step 1530, a criterion for accepting the response is evaluated. For example, the measured response tidal volume must be within a fixed percentage (e.g., 5%) of the target tidal volume of step 1505. If the criterion is not met, step 1535 is executed. In step 1535, the stimulation waveform is adjusted. If the criterion is met in step 1530, step 1540 is executed. In step 1540, the waveform parameters are stored for increased tidal volume at increased respiratory rate. In step 1545, the stimulation waveform parameters are established.

In step 1550, in use the system 100 is programmed to achieve increases and decreases in minute ventilation or other related parameters. The system 100 is then used to manipulate PCO₂ or SaO₂ levels by controlling minute ventilation or related respiration parameters that affect minute ventilation. Blood gas levels may be manipulated to prevent breathing disorders by stimulating the diaphragm after detecting a precursor to a breathing disorder. Examples of such detection and stimulation schemes are set forth in U.S. patent application entitled “Breathing Disorder and Precursor Predictor and Therapy Delivery Device and Method”, Tehrani, et al., and incorporated herein by reference. The stimulation waveforms may also be used to control oxygen saturation levels to treat heart failure patients, for example, periodically increasing oxygen saturation levels may be therapeutic to heart failure patients by either reducing the load on the heart and/or by having the patient breathe in a more advantageous manner. Examples of such breathing therapies and therapy devices are described in U.S. patent application entitled “Breathing Therapy Device and Method”, Tehrani, filed on even date herewith and incorporated in its entirety herein by reference.

FIG. 16 shows a stimulation waveform diagram in accordance with the invention. A stimulation waveform 1600 comprises an inspiration stimulus 1605 and an exhalation bias waveform 1610. The inspiration stimulus 1605 is applied for the duration that a diaphragm stimulation has typically been applied. The exhalation bias waveform 1610 comprises a first tapering component 1608 followed by low level biased portion 1609. The exhalation bias waveform 1610 may be characterized by a frequency f₀ and an amplitude A₀.

In known diaphragm stimulation the diaphragm is allowed to relax completely during exhalation. This relaxation typically begins at the end of the inspiration stimulus and results in a minimum volume being established for the lungs and airways. By applying a low-level bias stimulus to the diaphragm during all or part of the rest period, an enhanced negative intraplural pressure may be produced.

The enhanced negative pressure may used to increase the minimum volume for the lungs and airways. In certain circumstances it is believed that a greater minimum volume may relieve some of the gas exchange problems seen in disease states at lower resting lung volumes. The exhalation bias waveform 1610 provides a tool for modifying the lung volume during exhalation phase and rest period.

The exhalation bias waveform 1610 may be used to decrease the tidal volume, which may be used to decrease the minute ventilation and produce an increase in the partial pressure of CO₂.

In order to provide a smooth transition in the exhalation phase, the exhalation waveform component 1610 containing the first taper portion 1608 which comprises a negative ramp. The portion 1608 may be used to taper the exhalation. The low level bias stimulus portion 1609 provides a continuous low level enhanced negative intraplural pressure. The portion 1609 may be applied all or a portion of an exhalation period.

The stimulation device may be used, for example in subjects with breathing disorders, heart failure patients and patients who cannot otherwise breathe on their own such as spinal cord injury patients.

Safety mechanisms may be incorporated into any stimulation device in accordance with the invention. The safety feature disables the device under certain conditions. Such safety features may include a patient or provider operated switch, e.g., a magnetic switch. In addition a safety mechanism may be included that determines when patient intervention is being provided. For example, the device will turn off if there is diaphragm movement sensed without an EMG as the case would be where a ventilator is being used.

While the invention has been described in detail with reference to preferred embodiments thereof, it will be apparent to one skilled in the art that various changes can be made, and equivalents employed, without departing from the scope of the invention.

1.25. (canceled)

26. A method of treating a cardiovascular disorder comprising:
   stimulating tissue to elicit a diaphragm response to manipulate blood gas levels to thereby reduce a load on the heart.

27. The method of claim 26 wherein the stimulation is configured to elicit a diaphragm response to thereby increase SAO2 levels for a predetermined period of time.

28. The method of claim 27 wherein the stimulation is provided periodically wherein the heart is remodeled.

29. A method for treating a subject having a disorder characterized by a lower resting lung volume comprising:
   stimulating tissue to elicit a diaphragm response to thereby increase volume during a non-inspiratory phase.

30. The method of claim 29 wherein the step of stimulating tissue comprises:
   stimulating tissue to improve gas exchange.

31. The method of claim 29 wherein the step of stimulating comprises stimulating with an exhalation bias waveform.

32. A diaphragm stimulation device for use with a ventilator:
   wherein the device is configured to stimulate tissue of a subject to elicit a diaphragm response;
   wherein the device comprises a sensor configured to sense diaphragm EMG and a device configured to sense diaphragm movement; and
wherein the device is configured to turn off diaphragm stimulation when diaphragm movement is sensed in the absence of sensing a diaphragm EMG.

33. A system for diaphragm stimulation to elicit a minute ventilation different from the normal respiratory minute ventilation, comprising:
a programmable stimulation device for stimulating tissue of a subject to thereby elicit diaphragm response;
a sensor configured to sense a respiration parameter corresponding to a normal minute ventilation;
wherein said programmable stimulation device is programmable to provide a stimulation waveform to said diaphragm to elicit a minute ventilation different from the normal respiratory minute ventilation.

34. The system of claim 33, wherein said sensor is configured to sense a parameter corresponding to tidal volume.

35. The system of claim 33, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to respiratory tidal volume that is less than said normal tidal volume.

36. The system of claim 33, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to respiratory tidal volume that is greater than said normal tidal volume.

37. The system of claim 33, wherein said sensor is configured to sense a respiration parameter corresponding to a normal inspiration duration.

38. The system of claim 33, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to a normal inspiration duration associated with a normal respiratory rate.

39. The system of claim 33, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to an inspiration duration associated with a decreased respiratory rate.

40. The system of claim 33, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to an inspiration duration associated with an increased respiratory rate.

41. A method for providing a decreased minute ventilation in a subject with a programmable stimulation device coupled to tissue, said method comprising:
observing a normal tidal volume and a normal respiratory rate of said subject;
determining stimulation waveform parameters for producing a normal respiratory rate and a decreased tidal volume in said subject;
Storing said stimulation waveform parameters in said programmable device; and
applying a waveform stimulus to said tissue to elicit a diaphragm response wherein said waveform stimulus is characterized by said stimulation waveform parameters.

42. A method for providing an increased minute ventilation in a subject with a programmable stimulation device coupled to tissue of the subject, said method comprising:
observing a normal tidal volume and a normal respiratory rate of said subject;
determining stimulation waveform parameters for producing a normal respiratory rate and an increased tidal volume in said subject;
Storing said stimulation waveform parameters in said programmable device; and
applying a waveform stimulus to said tissue to elicit a diaphragm response wherein said waveform stimulus is characterized by said stimulation waveform parameters.

43. A method of respiration therapy comprising:
increasing minute ventilation with respect to a baseline minute ventilation by providing stimulation to elicit a diaphragm activation to increase one or more of a respiration rate, an inspiration duration, and a ratio of inspiration duration with respect to a corresponding respiration cycle duration.

44. A method for providing a decreased minute ventilation in a subject with a programmable stimulation device coupled to a tissue of the subject, said method comprising:
observing a normal tidal volume and a normal respiratory rate of said subject; determining stimulation waveform parameters for producing a decreased respiratory rate and a normal tidal volume in said subject;
Storing said stimulation waveform parameters in said programmable device; and applying a waveform stimulus to said tissue to elicit a diaphragm response, wherein said waveform stimulus is characterized by said stimulation waveform parameters.

45. A method for establishing a baseline minute ventilation for a subject with an implanted programmable diaphragm stimulation device, said method comprising:
attaching a flow sensor to said subject; observing a normal tidal volume and a normal respiratory rate;
measuring and storing data concerning the respiration of said subject; and determining a normal inspiration duration.

46. The method of claim 45, wherein said observing a normal tidal volume and normal respiratory rate of said subject comprises interacting with said subject while said subject is in a waking state.

47. The method of claim 45, wherein said observing a normal tidal volume and normal respiratory rate of said subject comprises observing said subject while said subject is in a sleeping state.

48. The method of claim 45, further comprising collecting respiratory gas composition data.

49. The method of claim 45, wherein said determining a normal inspiration duration comprises calculating an average.

50. The method of claim 45, further comprising collecting blood gas composition data.

51. A respiration stimulation device to change minute ventilation with respect to a baseline minute ventilation comprising:
at least one electrode configured to be coupled to tissue of a subject;
a signal source coupled to the electrode and configured to deliver a stimulation signal to the tissue to control breathing;
wherein the signal source is configured to control at least one parameter corresponding to minute ventilation to change minute ventilation with respect to a baseline minute ventilation.

52. The device of claim 51 wherein the signal source is configured to increase minute ventilation with respect to the baseline minute ventilation.

53. The device of claim 51, wherein the signal source is configured to decrease minute ventilation with respect to the baseline minute ventilation.
54. A system for diaphragm stimulation to elicit a tidal volume different from a normal respiratory tidal volume, comprising:
   a programmable stimulation device for stimulating tissue of a subject to thereby elicit diaphragm response;
   a sensor configured to sense a respiration parameter corresponding to a normal tidal volume;
   wherein said programmable stimulation device is programmable to provide a stimulation waveform to said diaphragm to elicit a tidal volume different from a normal respiratory tidal volume sensed by said sensor.

55. The system of claim 54, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to respiratory tidal volume that is less than said normal tidal volume.

56. The system of claim 54, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to respiratory tidal volume that is greater than said normal tidal volume.

57. The system of claim 54, wherein said sensor comprises a flow sensor configured to be coupled to a programmer.

58. The system of claim 54, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to a normal inspiration duration associated with a normal respiratory rate.

59. The system of claim 54, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to an inspiration duration associated with a decreased respiratory rate.

60. The system of claim 54, wherein said programmable stimulation device is programmable to provide a stimulation waveform to said tissue corresponding to an inspiration duration associated with an increased respiratory rate.

61. A method of providing respiratory therapy comprising:
   providing an electrical stimulator configured to stimulate tissue to activate a portion of a diaphragm comprising:
   stimulating tissue during exhalation to activate at least a portion of a diaphragm in a manner that increases end expiratory lung volume.

62. A method for treating a subject with a breathing disorder comprising the step of:
   electrically stimulating tissue of a patient to elicit a diaphragm response, wherein the step of electrically stimulating tissue comprises:
   electrically stimulating tissue of the subject during a non-inspiratory phase of a respiration cycle.

63. The method of treating a patient of claim 62 wherein the step of treating a patient comprises treating a patient having a disease state characterized at least in part by a gas exchange problem seen in the disease state at a lower resting lung volume.

64. The method of treating a patient of claim 62 wherein the step of treating a patient with a breathing disorder comprises treating a patient with apnea.

65. The method of treating a patient of claim 62 wherein the step of treating a patient with a breathing disorder comprises treating a patient with an obstructive breathing disorder.

66. The method of treating a patient of claim 62 wherein the step of treating a patient with a breathing disorder comprises treating a patient with hyperventilation.

67. The method of treating a patient of claim 62 wherein the step of treating a patient with a breathing disorder comprises treating a patient with hypoventilation.

68. The method of treating a patient of claim 62 wherein the step of treating a patient with a breathing disorder comprises treating a patient with partial apnea.

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