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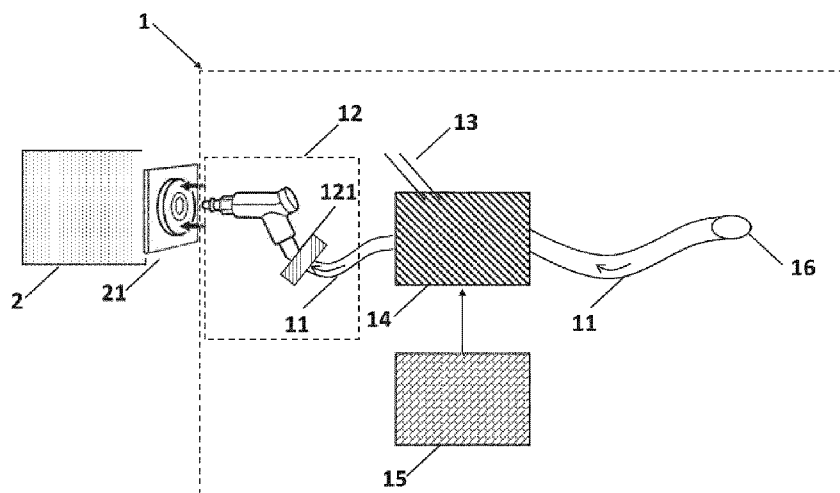


FIG. 1

(57) Abstract: The present invention relates to a portable tracheobronchial-air stimulation device (1) intended to be connected to a subject comprising a physiological interface (16); a vacuum interface (12), said vacuum interface (12) comprising a safety element (121); a vent (13); an electro-valve (14); and a control module (15) configured to control said electro-valve (14). The present invention also relates to a method for stimulating tracheobronchial-air.



HOSPITAL DEVICE FOR STIMULATING TRACHEOBRONCHIAL AIR

FIELD OF INVENTION

The present invention pertains to the field of the treatment of obstructive ventilatory disorders. In particular, the invention relates to a device for stimulating mucus to improve its expectoration.

BACKGROUND OF INVENTION

In the healthy individual, the lungs are covered by a “film” called mucus, whose thickness is a few millimeters and is very fluid. The function of this mucus is to protect the lung cells by isolating them from direct contact with air inspired by the lungs. The renewal of this mucus is ensured by cilia, mobile excrescences lying on the surface of the bronchi. These cilia, called vibratory, beat towards the proximal part of the airways, eliminating the inhaled particles trapped in the gel phase of the mucus which particles slide on the layer of cilia, like a conveyor belt. The clearance (the capacity of a mucociliary tissue, organ or organism to eliminate a substance from a given fluid) is carried out at a speed of 5 mm/min in the trachea, ensuring the renewal of the mucus layer every 20 minutes or so. This mucociliary clearance thus eliminates mucus to the pharynx where it will be swallowed or expectorated.

Various pathologies, such as cystic fibrosis, chronic obstructive pulmonary disease (COPD), pulmonary emphysema or chronic bronchitis, bronchiolitis, primary ciliary dyskinesia (*e.g.* KARTAGENER syndrome), bronchial stenosis, or sinusitis, result in an obstructive ventilatory disorder or pulmonary obstructive syndrome. These pathologies are characterized by an accumulation of mucus and result in a limitation of flow rates in the respiratory tract and by an increase in air resistance.

The resulting accumulation of bronchial mucus, because of its stagnation, is responsible for infections that can lead to serious pulmonary complications. Thus, it is necessary to perform a regular uncluttering of the lungs of patients suffering from those pathologies.

For a long time, attempts have been made to use mucolytics or mucoregulators.

5 Unfortunately, they have shown low medical results and the treatments used nowadays are often limited to the administration of bronchodilators and respiratory physiotherapy sessions. This treatment, whose purpose is to avoid the superinfection, can be traumatic for the patient and remains of limited effectiveness when the mucus is too viscous or elastic. In order to assist patients during this treatment, various devices to facilitate the expulsion of mucus have
10 been developed.

Such devices stimulate the tracheobronchial air of a patient by using powerful pulsations of air, vibrations of air, or positive/negative pressures. All these devices generate pressure variations during inspiration. The aim of those devices is to cause the patient to cough in order to dislodge the mucus, resulting in its expectoration. These devices have the
15 disadvantage of causing expectoration, that is to say a cough, during the expiration of the patient. This implies a traumatic experience for the patient and a risk of collapse of the bronchial walls if the negative pressure is not sufficiently small in amplitude and of short duration.

There is thus a need for a device able to stimulate tracheobronchial air that does not involve
20 expectoration.

There is also a need for a portable and autonomous device suitable for hospital use, *i.e.* easily installable and usable in a hospital room.

The Applicant has found that this need could be met with a device allowing passive expiration while improving the fluidification of the mucus. Indeed, the non-involvement of the
25 respiratory muscles during expiration, due to passive expiration, avoids collapse.

SUMMARY

The present invention relates to a portable tracheobronchial-air stimulation device intended to be connected to a subject comprising:

- (i) a physiological interface able to interface the device with the subject's airways;
- 5 (ii) a vacuum interface able to interface with a wall inlet of a medical vacuum system, said vacuum interface comprising a safety element;
- (iii) a vent;
- (iv) an electro-valve connected to said physiological interface, said vacuum interface and said vent; and
- 10 (v) a control module configured to control said electro-valve for the application of pressure oscillations at a frequency of at least 1 Hz, and set a negative pressure into the physiological interface.

In one embodiment, the tracheobronchial-air stimulation device does not comprise a negative pressure generator. In one embodiment, the control module is configured to control the
15 electro-valve for the application of an expiration cycle comprising a plurality of successive expirations, each expiration having a frequency and a duty cycle, said expiration cycle comprises a first part of an expiration cycle having a first frequency and a first duty cycle, and a second part of an expiration cycle having a second frequency and a second duty cycle, wherein the first part of the expiration cycle comprises a plurality of expirations having a
20 frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8. In one embodiment, the first part of an expiration cycle comprises a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a frequency of 6 Hz and a duty cycle of the
25 order of 0.6. In one embodiment, the control module is configured to adapt the expiration cycle previously chosen by the operator or the subject according to the results of evaluated average stimulation duration. In one embodiment, the control module is configured to receive instructions from the subject or operator to adjust the amplitude of the departing negative

pressures according to their tolerance. In one embodiment, the electro-valve is connected to the physiological interface via a connecting tube and/or the electro-valve is connected to the vacuum interface via a connecting tube. In one embodiment, the safety element is a safety tube having an inner diameter less than 5 mm and a length greater or equal to 1 cm and less
5 or equal to 10 cm. In one embodiment, the pressure oscillations are applied during the expiratory phase of the subject .

The present invention also relates to a method for stimulating tracheobronchial-air comprising the steps of:

- (i) providing a tracheobronchial-air stimulation device according to the invention;
- 10 (ii) connecting the vacuum interface with a wall inlet of a medical vacuum system;
- (iii) connecting said tracheobronchial-air stimulation device to a subject via the physiological interface;
- (iv) applying an expiration cycle comprising a plurality of successive expirations to the subject, each expiration having a frequency and a duty cycle,
- 15 wherein the expiration cycle comprises a first part of an expiration cycle having a first frequency and a first duty cycle, and a second part of an expiration cycle having a second frequency and a second duty cycle.

In one embodiment, the tracheobronchial-air stimulation device does not comprise a negative pressure generator. In one embodiment, the first part of the expiration cycle comprises a
20 plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8. In one embodiment, the first part of an expiration cycle comprises a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a frequency
25 of 6 Hz and a duty cycle of the order of 0.6. In one embodiment, the control module is configured to adapt the expiration cycle previously chosen by the operator or the subject according to the results of evaluated average stimulation duration. In one embodiment, the control module is configured to receive instructions from the subject or operator to adjust the

amplitude of the departing negative pressures according to their tolerance. In one embodiment, the electro-valve is connected to the physiological interface via a connecting tube and/or the electro-valve is connected to the vacuum interface via a connecting tube.

5 DEFINITIONS

In the present invention, the following terms have the following meanings:

- **“Subject”** refers to a subject receiving a tracheobronchial-air stimulation using the device of the invention. The terms “subject” and “patient” can be used interchangeably herein.
- **“Expiration cycle”** refers to a plurality of successive expirations applied to a subject during a treatment session.
- **“Frequency”** refers to the number of depressions per expiration divided by the duration of the same expiration.
- **“Duty cycle”** refers to the time interval within an expiration during which the negative pressure is maintained. The duty cycle defines the relationship between the time during which negative pressure is applied to the subject and the total duration of an expiration. In other words, this duty cycle corresponds to the time during which the subject’s lungs are subjected to negative pressure during an expiration.

DETAILED DESCRIPTION

- The following detailed description will be better understood when read in conjunction with the drawings. For the purpose of illustrating, the device is shown in the preferred embodiments. It should be understood, however that the present invention is not limited to the precise arrangements, structures, features, embodiments, and aspect shown. The drawings are not drawn to scale and are not intended to limit the scope of the claims to the embodiments depicted. Accordingly, it should be understood that where features mentioned in the appended claims are followed by reference signs, such signs are included solely for the

purpose of enhancing the intelligibility of the claims and are in no way limiting on the scope of the claims.

This invention relates to a portable tracheobronchial-air stimulation device intended to be connected to a subject.

5 Said tracheobronchial-air stimulation device comprises:

- (i) a physiological interface able to interface the device with the subject's airways;
- (ii) a vacuum interface able to interface with a wall inlet of a medical vacuum system, said vacuum interface comprising a safety element;
- (iii) a vent;
- 10 (iv) an electro-valve connected to said physiological interface, said vacuum interface and said vent; and
- (v) a control module configured to control said electro-valve for the application of pressure oscillations at a frequency of at least 1 Hz, and set a negative pressure into the physiological interface.

15 The subject typically suffers from an obstructive ventilatory disorder and the device of the invention is able to modify the rheology of his tracheobronchial mucus.

Herein, the expression “obstructive ventilatory disorders” includes pathologies such as for example cystic fibrosis, chronic obstructive pulmonary disease (COPD), pulmonary emphysema or chronic bronchitis, bronchiolitis, primary ciliary
20 dyskinesia (*e.g.* KARTAGENER syndrome), bronchial stenosis, but also extends to disorders associated with nasal obstruction, such as sinusitis. Sinusitis corresponds to sinus obstruction following inflammation of the mucous membranes of the nose resulting in altered drainage of the nasal mucus.

The device targets the bronchial mucus and therefore aims at the stimulation of
25 intra-pulmonary air in order to offer the possibility of a passive expiration while improving the fluidification of the mucus.

The control module is configured to control said electro-valve for the application of pressure oscillations, at a frequency of at least 1 Hz, preferably during the expiratory phase, so that the subject is active. This advantageously creates pressure oscillations during the expiratory phase to mechanically stimulate mucus in the airway of the subject, thereby facilitating mucus fluidification and drainage.

The control module is configured to control said electro-valve for the application of pressure oscillations, at a frequency of at least 1 Hz for mucus fluidification and drainage, preferably at least 4 Hz advantageously for mucus drainage, more preferably at least 10 Hz advantageously for mucus fluidification.

10 In particular, the device aims at aspirating air from the subject's lungs during a cycle comprising a plurality of expirations, said subject being passive. Said expiration cycle comprises a plurality of successive expirations, each expiration having eventually distinct parameters such as frequency and duty cycle. It has to be noted that during one expiration, the frequency and duty cycle are kept constant. Typically, an expiration cycle can be divided
15 into 2 parts: a first part comprises n_1 successive expirations with a frequency f_1 and a duty cycle D_1 , then a second part comprises n_2 successive expirations with a frequency f_2 and a duty cycle D_2 , n_1 and n_2 being positive integers. Frequencies f_1 and f_2 refer to the frequency of pressure oscillations. The purpose of the first part of the expiration cycle is to fluidify and dislodge the mucus accumulated in a subject's lungs, while the purpose of the second part of
20 the same expiration cycle is to evacuate said mucus from the subject's lungs. The number of expirations per expiration cycle is predetermined by the operator or the subject.

The passive expiration performed with the device of the present invention can provide an expiratory aid, which will increase expiratory time. The expiration is ensured by the device, thus passive for the subject, which avoids the physiological bronchial collapse which is a
25 major obstacle to the uncluttering of the airways. This prolonged expiration allows reaching the peripheral airways, which are usually the main "target" of the uncluttering maneuvers.

The uncluttering of the subject's airways is thus more effective than when using active expiration.

Furthermore, the tracheobronchial-air stimulation device is a compact device configured to have an external negative pressure source. Advantageously, this allows the tracheobronchial-air stimulation device to be portable and installed at any locations, provided that a medical vacuum system is available.

A portable device refers to a device that the patrician can hold in his hand and carry with him at all times (for example in his pocket or in a small briefcase), and that he can move to the patient (wherever said patient is in the hospital, provided there is access to the medical vacuum system). In this case, the patient does not need to move.

On the contrary, artificial respiration apparatus and ventilators are not portable devices. Indeed, they are bulky devices because they contain pumps and gas cylinders. In this case, they have a dedicated location in the hospital, and the patient must be brought to the device.

The medical vacuum system may be a central medical vacuum supply, *i.e.* vacuum is available from wall inlets (pipeline) located in a healthcare facility, such as for example a hospital; as such it may also be called "intramural vacuum system". The vacuum is created by running a mechanical pump like a compressor, but instead of creating a high pressure in the pump and sending that compressed gas to a receiver tank, this pump sucks the gases out of the receiver tank and forces the compressed air outside leaving a vacuum in the receiving tank that is connected to the house piping. The major source of vacuum is typically a pump, typically located in the basement of the building.

The medical vacuum system generates and delivers high vacuum at the vacuum inlet. Said high vacuum is applied to the device when said device is connected to the vacuum inlet via the vacuum interface. The control module of the device then controls the electro-valve to set a desired negative pressure to be delivered to the subject via the physiological interface. In

other words, the medical vacuum system works as a vacuum provider for the device allowing said device to deliver negative pressure impulses to the lungs of a subject.

According to one embodiment, the medical vacuum system generates a vacuum ranging from 0 mbar to -900 mbar, preferably from -200 mbar to -400 mbar, more preferably
5 from -150 mbar to -400 mbar.

The safety element is configured to protect the fragile lungs of the subject from the vacuum generated from the medical vacuum system. Indeed, said vacuum is very strong and could damage the lungs of the subject if no valve is included in the device.

According to one embodiment, if the vacuum generated by the medical vacuum system is too
10 strong and results in a negative pressure too strong for the lungs to support it, the risk of lungs crushing being high, the safety element is then configured to close and thus stop immediately the expiration.

In a specific configuration of this embodiment, the safety element is a safety valve configured to close and stop immediately the expiration cycle if the vacuum generated at the wall inlet
15 exceeds a critical threshold of -300 mbar. For example, the vacuum can exceed this critical threshold because of a malfunction of the manometer, or a bad user setting.

In an alternate configuration of this embodiment, the safety element is a safety valve is configured to close and stop immediately the expiration cycle if the negative pressure generated by the device exceeds a critical threshold of -70 mbar. Indeed, if the negative
20 pressure applied to the lungs exceeds a critical threshold of -70 mbar, it becomes uncomfortable for the subject. In the same way, if the oscillatory flow exceeds a critical threshold of 180 L/min, the safety valve is then configured to close and thus stop immediately the expiration.

Preferably, the safety valve is a solenoid valve.

In an alternate configuration of this embodiment, the safety element is configured to modify the vacuum range delivered to the device by the medical vacuum system. For example, the medical vacuum system generates a vacuum between -150 mbar and -450 mbar, and the safety element modifies this range to be between -200 mbar and -150 mbar by applying air
5 leaks.

In another embodiment, the safety element may be a safety tube connecting the vacuum interface to the wall inlet. Said safety tube has an inner diameter less than 5 mm and a length greater or equal to 1 cm and less or equal to 10 cm, preferably less or equal to 5 cm. In a preferred configuration, the safety tube has an inner diameter ranging from 4 mm to 5 mm
10 and a length ranging from 1.5 cm to 2.5 cm. The safety tube advantageously modifies the vacuum range delivered to the device by the medical vacuum system, in particular the safety tube lowers said vacuum range to protect the lungs of the subject from any damage from a too strong vacuum.

Preferably, the tracheobronchial-air stimulation device does not comprise a negative pressure generator as it uses medical vacuum system as an external negative pressure source.
15

According to one embodiment, the device generates an oscillatory flow rate during the patient's exhalation ranging from 20 L/min to 200 L/min, preferably from 30 L/min to 180 L/min, this oscillatory flow rate is correlated to the pressure oscillations.

According to one embodiment, negative pressure ranges from -10 mbar to -60 mbar.

20 According to one embodiment, the physiological interface comprises a mouthpiece or a breathing mask. Thus, the physiological interface will connect with the mouth, or the mouth and the nose of the subject wearing it.

In a preferred embodiment, said physiological interface is equipped with an RFID tag for tracking the subject.

According to one embodiment, the device comprises a connecting tube connecting the electro-valve to the physiological interface, said connecting tube being preferably flexible.

According to one embodiment, the device comprises a connecting tube connecting the electro-valve to the vacuum interface, said connecting tube being preferably flexible.

- 5 According to one embodiment, the control module is configured to adapt the expiration cycle previously chosen by the operator or the subject according to the results of evaluated average stimulation duration.

According to one embodiment, the control module is configured to receive instructions from the subject or operator to adjust the amplitude of the departing negative pressures according
10 to their tolerance.

According to one embodiment, the expiration cycle comprises a plurality of expirations, each expiration having distinct parameters such as frequency and duty cycle.

According to one embodiment, the control module is configured to control the application of a succession of alternation of negative pressure and venting defining at least one duty cycle.

- 15 According to one embodiment, the control module is configured to control the application of a succession of negative pressure defining at least one frequency.

In one embodiment, said control module comprises a pressure sensor which is connected to the vacuum interface via a tube. In addition, said pressure sensor advantageously takes the form of a relative pressure sensor measuring the value of the vacuum with respect to the
20 ambient atmospheric pressure. On this type of sensor, pressure fluctuations due to weather or altitude changes have a direct impact on the measured value. If the pressure exerted on the relative pressure sensor is lower than the ambient pressure, it is called negative relative pressure and the value is preceded by a sign "-".

Relative pressure sensors have a well-known structure and typically only have one pressure
25 connection. The ambient pressure is exerted through a slot or a vent tube located at the rear

of the sensor membrane and this relative measurement is compensated for. The applicant has been able to demonstrate that the negative pressure has to be maintained within a specific time interval, defined herein as duty cycle, within an expiration in order to optimize the efficiency of the treatment and avoid the variability between subjects. The control of this time makes it possible to avoid a too long expiratory time that could lead to a collapse of the bronchi. In addition, this modulation of the duty cycle of each negative pressure makes it possible, beyond the negative pressure generated which has a shearing action on the bronchial mucus and which therefore causes its viscosity to drop, to apply a flow that is longer or shorter, which improves the secretions transport. More specifically, it is important that the negative pressure applied to the tracheobronchial mucus be between -40 and -100 millibars, preferably between -45 and -80 millibars, and preferably between -30 and -70 millibars.

Preferably, the electro-valve is a solenoid valve which has a closing rate inferior to 5 ms. Said closing rate refers to the time between the issuance of the closing command and the effective closing of the valve.

According to one embodiment, the electro-valve is configured to tune the negative pressure amplitude by mixing the strong negative pressure provided by the medical vacuum system and the atmospheric pressure using the opening and closing of the vent.

According to one embodiment, the device further comprises a microcontroller. In this embodiment, the control module has the advantage of being able to vary the fluidification effect of the device via said microcontroller which controls the switching frequency of the electro-valve and the opening and closing times of the electro-valve. In particular, depending on the negative pressure measured by the pressure sensor and the operator-determined parameters, the microcontroller is able to control the electro-valve to mix the strong negative pressure provided by the medical vacuum system and the atmospheric pressure by opening and/or closing the vent in order to obtain a desired amplitude of negative pressure applied to the tracheobronchial mucus of the subject. The operator-determined parameters are within a range defined by a set of desirable parameters stored in the memory associated with the

microcontroller. Preferably, the microcontroller is able to tune the negative pressure applied to the tracheobronchial mucus of the subject between -10 and -100 millibars, preferably between -15 and -70 millibars, more preferably between -20 and -60 millibars. In this way, the treatment applied to the subject by the device will achieve optimal efficiency and limit the impact of interpatient variability.

According to one embodiment, the first part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 for mucus fluidification and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8 for mucus drainage.

In a preferred configuration of this embodiment, the first part of an expiration cycle comprises a plurality of expirations having a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of 6 Hz and a duty cycle of the order of 0.6.

According to one embodiment, the first part of an expiration cycle comprises a plurality of expirations ranging from 2 to 10 expirations, preferably from 4 to 8 expirations, more preferably 8 expirations and the second part of an expiration cycle comprises a plurality of expirations ranging from 1 to 5 expirations, preferably from 1 to 4 expirations, more preferably 2 expirations.

Preferably, the defined number of expirations is initially selected by the subject or operator and is adapted by the device according to the results of the evaluated average stimulation duration.

According to one embodiment, the microcontroller is configured to adapt the negative pressure to obtain a negative pressure applied to the tracheobronchial mucus of the subject of between -40 and -100 millibars, preferably between -45 and -80 millibars, preferably between -50 and -100 millibars to the respiratory tract of the subject. In particular, the

microcontroller is configured to control the switching frequency, the opening and closing times of the electro-valve and/or the vent.

According to one embodiment, the microcontroller is configured to also control the negative pressure provided by the device as a function of the measured duration of stimulation.

- 5 In one embodiment, the vacuum interface comprises a vacuum setting system located on the hospital room wall, said vacuum setting system is a vacuum regulator being configured to tune and/or to monitor the vacuum level. Said vacuum setting system will need to be calibrated before use. In this embodiment, the vacuum setting system may be a hospital manometer or a correspondence table comprising standard settings. Preferably, the vacuum
10 setting system is a pressure gauge.

In another embodiment, the vacuum interface does not comprise a vacuum setting system, but is connected to the vacuum inlet via an external vacuum setting system. In this embodiment, said vacuum setting system is not included in the device of the invention.

- In a specific configuration of both preceding embodiments, the vacuum inlet is connected to
15 the safety element of the vacuum interface via a vacuum setting system, providing this succession of elements: safety element – vacuum setting system - medical vacuum system.

- According to one embodiment, the device further comprises a stopwatch for determining the duration of expirations during which the successive negative pressures are applied to the subject. Said stopwatch has the advantage of assisting the expiration of the subject. Thus, for
20 an expiration to be effective, it is important for the stimulation to take place for a minimum period of at least five seconds and therefore for the expiration of subject to be maintained for at least this period. Indeed, a short time of stimulation of the subject during expiration materializes a low respiratory capacity and a descent into negative pressure too fast. This results in too strong suction of device that empties too quickly the subject's lung volume.

- 25 According to one embodiment, the device further comprises a calculator able to determine the average amplitude of negative pressure applied and the average duration of stimulation

during all expirations to the subject on the basis of the negative pressure amplitude and duration measured at each expiration.

Said calculator may store in its memory each command of the electro-valve, each value of the signal from the pressure sensor and representative of the amplitude of the vacuum
5 measured instantaneously and the number of control cycles of the electro-valve for the entire duration (determined by a scalable parameter stored by the apparatus) of the expiration cycle to allow the calculator by a calculation using the amplitude values and the expirations number to determine the average negative pressure amplitude measured at each expiration, then memorize and then determine the average negative pressure amplitude applied during all the
10 expirations performed by the subject during the expiration cycle. The calculator associated with the pressure sensor also measures during the time intervals when the electro-valve is closed so as not to apply a negative pressure impulse, the evolution of the pressure in the lung of the subject during the expiration and the time required to reach the pressure amplitude corresponding to an expiration and stored as a threshold in the device. Said time
15 corresponding to the duration of an expiration is stored and used by the device. This value representative of the duration of the expiration will be compared with a first threshold value, stored by the calculator which represents a value of minimum duration for the calculator to adjust the amplitude of negative pressure generated by the device when the representative value of the duration of an expiration drops below the minimum value set. A second threshold
20 value which represents a maximum duration of the expiration and stored by the calculator is used by the latter in comparison with the measured duration to generate a control signal of the increase of the negative pressure if the duration of the expiration measured exceeds the second saved value.

In some embodiments, the device includes a dead man remote control, which must be actively
25 and continuously actuated or regularly reset by the subject, during the treatment, for the device to operate. Otherwise, the device stops.

In a preferred embodiment, an internal power supply supplies the various components of the device such as the pressure sensor, the stopwatch and/or the microcontroller. In this embodiment, the internal power supply may be a battery.

5 In one embodiment, an external power supply supplies the various components of the device such as the pressure sensor, the stopwatch and/or the microcontroller.

In another aspect, the present invention relates to a method for stimulating tracheobronchial-air comprising the steps of:

- (i) providing a tracheobronchial-air stimulation device of the invention;
- (ii) connecting the vacuum interface with a wall inlet of a medical vacuum system;
- 10 (iii) connecting said tracheobronchial-air stimulation device to a subject via the physiological interface;
- (iv) applying an expiration cycle comprising a plurality of successive expirations to the subject, each expiration having a frequency and a duty cycle,

wherein the expiration cycle comprises a first part of an expiration cycle having a first
15 frequency and a first duty cycle, and a second part of an expiration cycle having a second frequency and a second duty cycle.

The tracheobronchial-air stimulation device is as described hereabove.

In one embodiment, after connecting the vacuum interface with a wall inlet of a medical vacuum system (step ii), the vacuum is regulated via a vacuum setting system.

20 In one embodiment, the first part of the expiration cycle comprises a plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8.

In a specific configuration of this embodiment, the first part of an expiration cycle comprises
25 a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a frequency of 6 Hz and a duty cycle of the order of 0.6.

While various embodiments have been described and illustrated, the detailed description is not to be construed as being limited hereto. Various modifications can be made to the embodiments by those skilled in the art without departing from the true spirit and scope of the disclosure as defined by the claims.

5

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 represents the tracheobronchial-air stimulation device according to one embodiment.

Figure 2 represents the tracheobronchial-air stimulation device connected to the subject.

10 **Figure 3A** represents an example of the negative pressure signals generated by the device when the vacuum level of the medical vacuum system is set to -150 mbar.

Figure 3B shows the negative pressure signals of figure 3A in the time range from 4 to 5 seconds.

15 **Figure 3C** represents an example of the flow rate signals generated by the device when the vacuum level of the medical vacuum system is set to -150 mbar.

Figure 3D shows the flow rate signals of figure 3C in the time range from 4 to 5 seconds.

Figure 4A represents an example of the negative pressure signals generated by the device when the vacuum level of the medical vacuum system is set to -200 mbar.

20 **Figure 4B** represents an example of the flow rate signals generated by the device when the vacuum level of the medical vacuum system is set to -200 mbar.

Figure 5A represents an example of the negative pressure signals generated by the device when the vacuum level of the medical vacuum system is set to -250 mbar.

Figure 5B represents an example of the flow rate signals generated by the device when the vacuum level of the medical vacuum system is set to -250 mbar.

Figure 6A represents an example of the negative pressure signals generated by the device when the vacuum level of the medical vacuum system is set to -300 mbar.

- 5 **Figure 6B** represents an example of the flow rate signals generated by the device when the vacuum level of the medical vacuum system is set to -300 mbar.

ILLUSTRATIVE EMBODIMENTS OF THE INVENTION

As shown in Figures 1 and 2, the tracheobronchial-air stimulation device **1** comprises:

- 10 (i) a physiological interface **16** interfacing the device with a subject's airways;
- (ii) a vacuum interface **12** interfacing with a wall inlet **21** of a medical vacuum system **2**, said vacuum interface **12** comprising a safety element **121**;
- (iii) a vent **13**;
- (iv) an electro-valve **14** connected to said physiological interface **16**, said vacuum interface **12** and said vent **13**; and
- 15 (v) a control module **15** configured to control said electro-valve **14** and set a negative pressure into the physiological interface **16**.

In this embodiment, vacuum is provided by the medical vacuum system **2**. The device **1** is connected to said medical vacuum system **2** by the wall inlet **21**. The vacuum interface **12** interfaces with said wall inlet **21** using a flexible pipe **11** to provide vacuum for the device **1**. The safety element **121** of the vacuum interface **12** is configured to ensure the safety of the subject's lungs in regard to the vacuum provided. If said vacuum is too strong and results in a negative pressure too strong for the lungs to support it, the risk of lungs crushing being high, the safety element **121** is a valve configured to close and thus stop the expiration. The control module **15** controls said electro-valve **14**, which opens and closes at a frequency chosen by the operator or the subject, and sets a negative pressure into the physiological

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interface **16** to ensure passive expiration cycles leading to the expectoration of mucus from the subject.

This embodiment is particularly advantageous as it allows passive expiration while improving the fluidification of the mucus. Indeed, the expiration is ensured by the device **1**,
5 thus passive for the subject, which avoids the physiological bronchial collapse which is a major obstacle to the uncluttering of the airways.

EXAMPLES

The present invention is further illustrated by the following examples.

Example 1: Validation test

10 A validation test was conducted on the device of the invention to ensure that said device is suitable for use on a subject. The validation test was not performed on a subject.

The validation criteria are the following:

- the negative pressure should stay within the interval of -300 mbar to -10 mbar;
- the flow rate should stay within the interval of 30 L/min to 180 L/min.

15 A device according to the invention is set up.

The vacuum interface is connected to the wall inlet of the medical vacuum system. The vacuum level from the medical vacuum system is tuned prior use.

The flow rate and negative pressure delivered by the device are then measured.

Flow rate measurements were performed in an open loop (physiological interface left open),
20 and negative pressure measurements were performed in a close loop (physiological interface obstructed). Measurements were performed ex vivo, *i.e.* not on a subject.

Table 1 below lists configurations in which experiments have been performed.

Vacuum level at wall inlet (mbar)	First part of the expiration cycle			Second part of the expiration cycle			Results (negative pressure and flow rate)	
/	Number of expirations (n1)	Frequency (Hz)	Duty cycle	Number of expirations (n2)	Frequency (Hz)	Duty cycle	Maximum negative pressure (mbar)	Maximum oscillatory flow rate (L/min)
-150	8	12	40%	2	6	40%	-81	63.9
-200	8	12	40%	2	6	40%	-136	76.2
-250	8	12	40%	2	6	40%	-155	85.5
-300	8	12	40%	2	6	40%	-175	96.1

Table 1

As observed on figures 3-6, the negative pressure stayed within the interval of:

- Lower limit: -300 mbar
- Upper limit: -30 mbar

The flow rate stayed within the interval of:

- Lower limit: 30 L/min
- Upper limit: 180 L/min

No deviations were observed during testing.

Figures 3B and 3D show the impulsions of negative pressure delivered by the device between 4 and 5 seconds. In this case, there were 12 impulsions in 1 second of experiment.

Thus, validation criteria were fully met in all experiments, indicating that the device of the invention is safe to use on a subject.

Example 2: Mucus evacuation

A device according to the invention is set up.

The vacuum interface is connected to the wall inlet of the medical vacuum system. The vacuum level from the medical vacuum system is tuned prior use.

The physiological interface is adapted on the subject.

The parameters of the expiration cycle (number of expirations, negative pressure, frequency, duty cycle) are set up by the operator or the subject.

Table 2 below lists configurations in which experiments have been performed.

Vacuum level at the wall inlet (mbar)	Negative pressure delivered by the device (mbar)	First part of the expiration cycle			Second part of the expiration cycle			Treatment efficiency
/	/	Number of expirations (n1)	Frequency (Hz)	Duty cycle	Number of expirations (n2)	Frequency (Hz)	Duty cycle	
-150	-50	8	12	40%	2	6	40%	Mucus evacuated
-150	-50	3	6	20%	5	4	30%	Mucus non evacuated

Table 2

With the first part of the expiration cycle comprising a plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of the expiration cycle comprising a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8, the mucus is efficiently evacuated.

This relies on the efficiency of the first part of the expiration cycle to fluidify the mucus, allowing the second part of the expiration cycle to drain the fluidified mucus.

When parameters such as frequency and duty cycle do not fall within the precited ranges, the mucus is not evacuated.

REFERENCES

- 1 – Tracheobronchial-air stimulation device
- 11 – Pipe
- 12 – Vacuum interface
- 121 – Safety element
- 13 – Vent
- 14 – Electro-valve
- 15 – Control module
- 16 – Physiological interface
- 2 – Medical vacuum system
- 21 – Wall inlet

CLAIMS

1. A portable tracheobronchial-air stimulation device (1) intended to be connected to a subject comprising:
 - (i) a physiological interface (16) able to interface the device (1) with the subject's airways;
 - (ii) a vacuum interface (12) able to interface with a wall inlet (21) of a medical vacuum system (2), said vacuum interface (12) comprising a safety element (121);
 - (iii) a vent (13);
 - (iv) an electro-valve (14) connected to said physiological interface (16), said vacuum interface (12) and said vent (13); and
 - (v) a control module (15) configured to control said electro-valve (14) for the application of pressure oscillations at a frequency of at least 1 Hz, and set a negative pressure into the physiological interface (16).
2. The tracheobronchial-air stimulation device (1) according to claim 1, which does not comprise a negative pressure generator.
3. The device (1) according to any one of claim 1 or 2, wherein the control module is configured to control the electro-valve for the application of an expiration cycle comprising a plurality of successive expirations, each expiration having a frequency and a duty cycle, said expiration cycle comprises a first part of an expiration cycle having a first frequency and a first duty cycle, and a second part of an expiration cycle having a second frequency and a second duty cycle, wherein the first part of the expiration cycle comprises a plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8.

4. The device (1) according to claim 3, wherein the first part of an expiration cycle comprises a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a frequency of 6 Hz and a duty cycle of the order of 0.6.
5. The device (1) according to any one of claims 3 to 4, wherein the control module (15) is configured to adapt the expiration cycle previously chosen by the operator or the subject according to the results of evaluated average stimulation duration.
6. The device (1) according to any one of claims 1 to 5, wherein the control module (15) is configured to receive instructions from the subject or operator to adjust the amplitude of the departing negative pressures according to their tolerance.
7. The device (1) according to any one of claims 1 to 6, wherein the electro-valve (14) is connected to the physiological interface (16) via a connecting tube (11) and/or the electro-valve (14) is connected to the vacuum interface (12) via a connecting tube (11).
8. The device (1) according to any one of claims 1 to 7, wherein the safety element is a safety tube having an inner diameter less than 5 mm and a length greater or equal to 1 cm and less or equal to 10 cm.
9. The device (1) according to any one of claims 1 to 8, wherein the pressure oscillations are applied during the expiratory phase of the subject.
10. A method for stimulating tracheobronchial-air comprising the steps of:
 - (i) providing a tracheobronchial-air stimulation device (1) according to any one of claims 1 to 9;
 - (ii) connecting the vacuum interface (12) with a wall inlet (21) of a medical vacuum system (2);
 - (iii) connecting said tracheobronchial-air stimulation device (1) to a subject via the physiological interface (16);

(iv) applying an expiration cycle comprising a plurality of successive expirations to the subject, each expiration having a frequency and a duty cycle, wherein the expiration cycle comprises a first part of an expiration cycle having a first frequency and a first duty cycle, and a second part of an expiration cycle having a second frequency and a second duty cycle.

11. The method according to claim **10**, wherein the tracheobronchial-air stimulation device (1) does not comprise a negative pressure generator.
12. The method according to any one of claim **10** or **11**, wherein the first part of the expiration cycle comprises a plurality of expirations having a frequency of the order of 10 to 15 Hz and a duty cycle of 0.2 to 0.7 and the second part of an expiration cycle comprises a plurality of expirations having a frequency of the order of 4 to 7 Hz and a duty cycle of the order of 0.5 to 0.8.
13. The method according to claim **12**, wherein the first part of an expiration cycle comprises a frequency of 12 Hz and a duty cycle of the order of 0.3 and the second part of an expiration cycle comprises a frequency of 6 Hz and a duty cycle of the order of 0.6.
14. The method according to any one of claims **10** to **13**, wherein the control module (15) is configured to adapt the expiration cycle previously chosen by the operator or the subject according to the results of evaluated average stimulation duration.
15. The method according to any one of claims **10** to **14**, wherein the control module (15) is configured to receive instructions from the subject or operator to adjust the amplitude of the departing negative pressures according to their tolerance.
16. The method according to any one of claims **10** to **15**, wherein the electro-valve (14) is connected to the physiological interface (16) via a connecting tube (11) and/or the electro-valve (14) is connected to the vacuum interface (12) via a connecting tube (11).

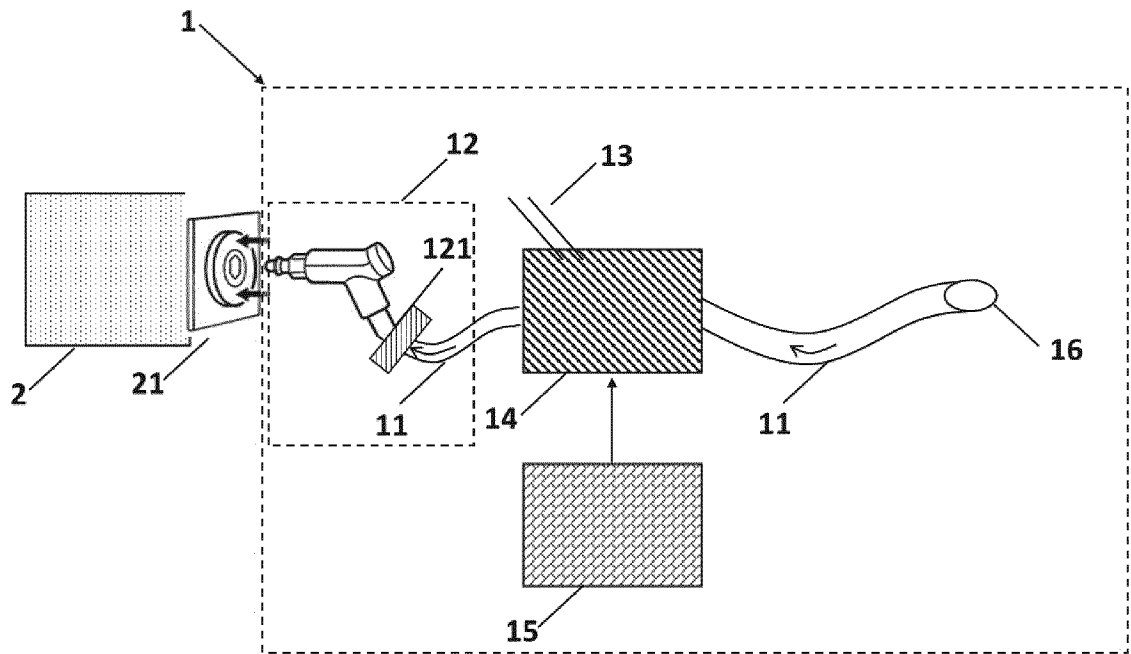


FIG. 1

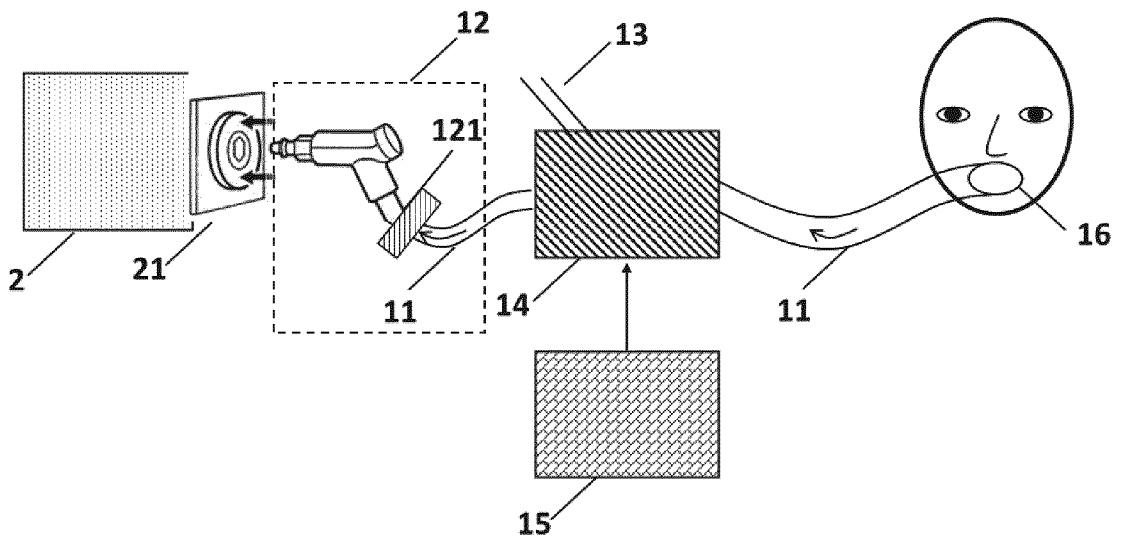


FIG. 2

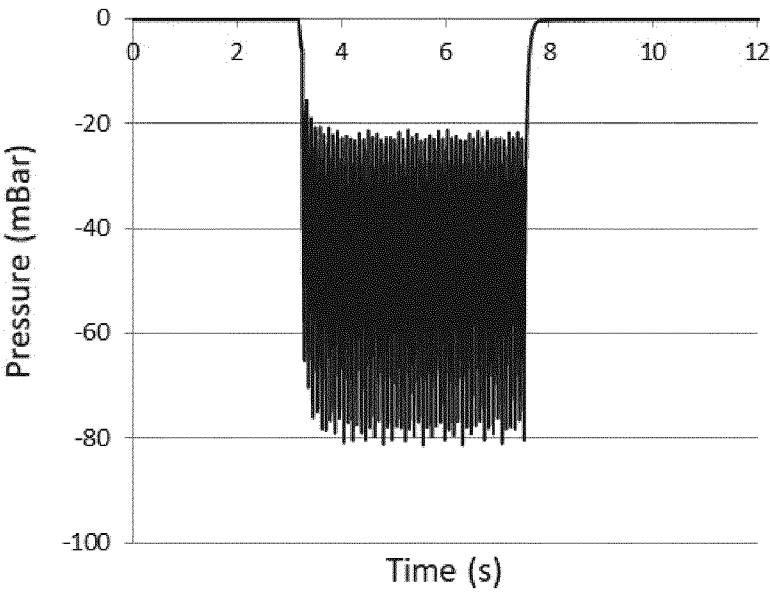


FIG. 3A

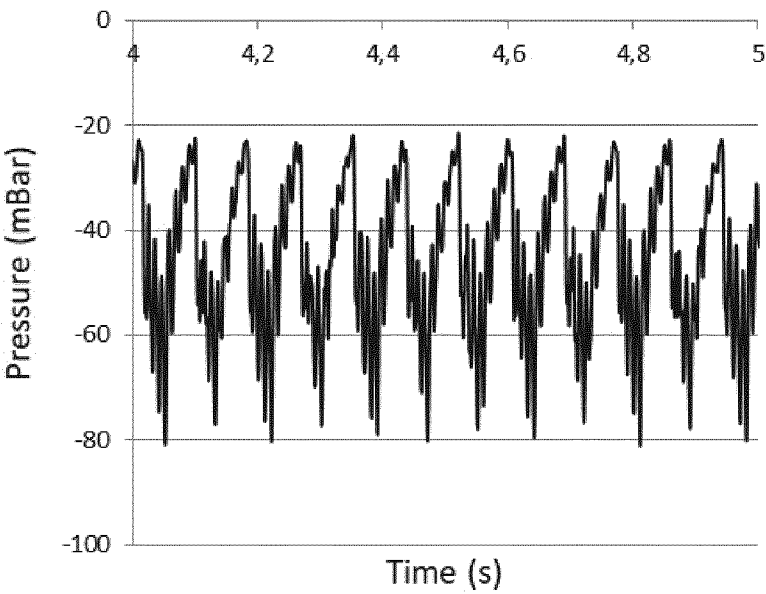


FIG. 3B

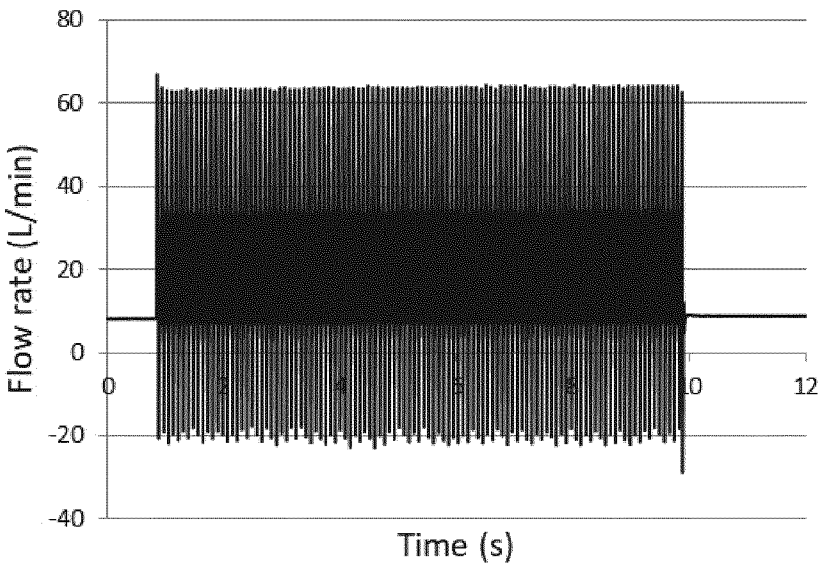


FIG. 3C

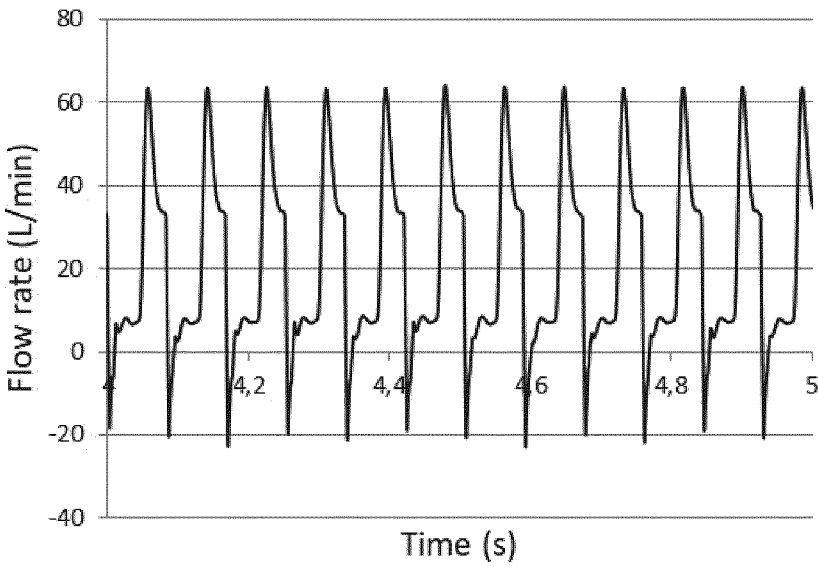


FIG. 3D

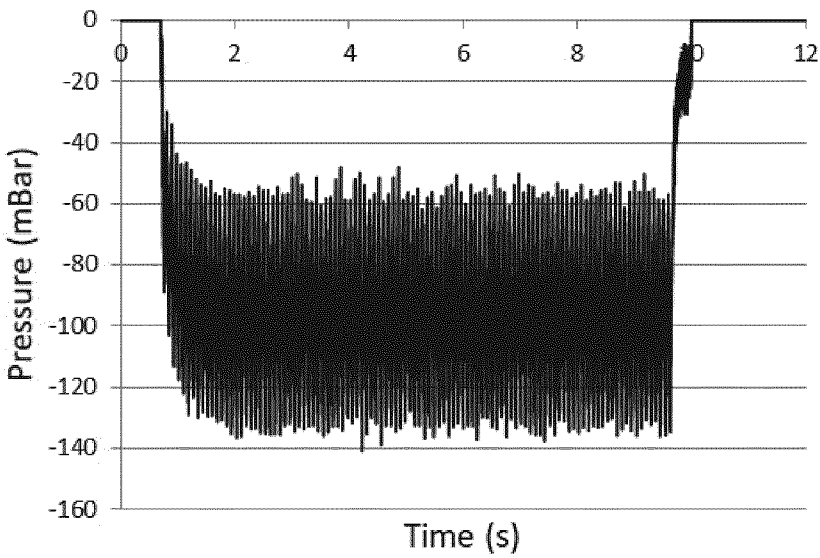


FIG. 4A

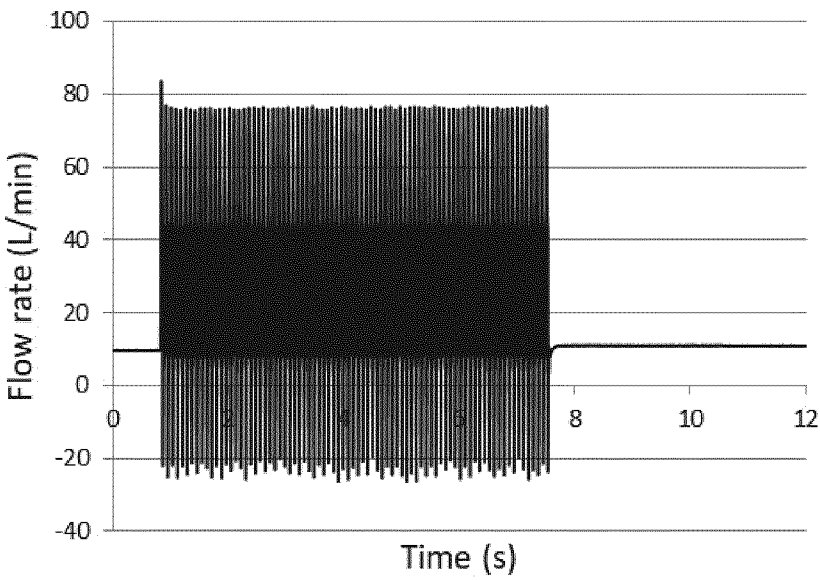


FIG. 4B

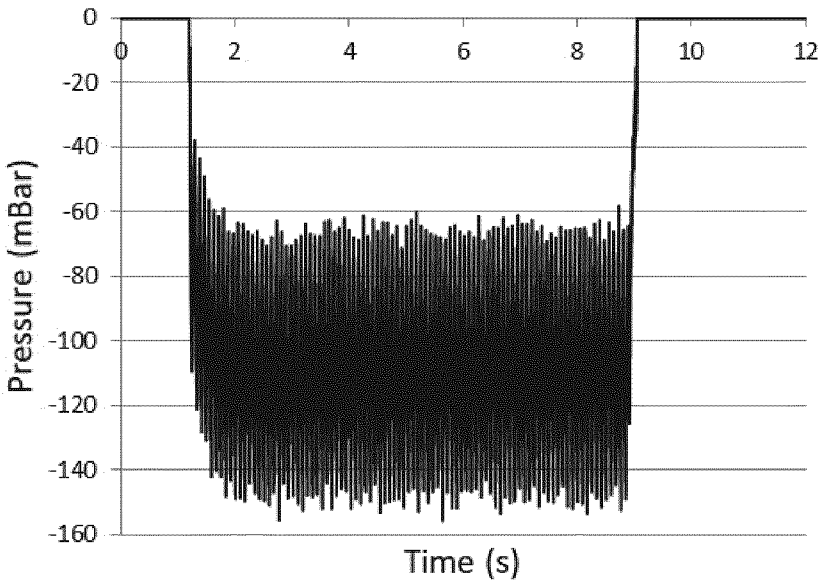


FIG. 5A

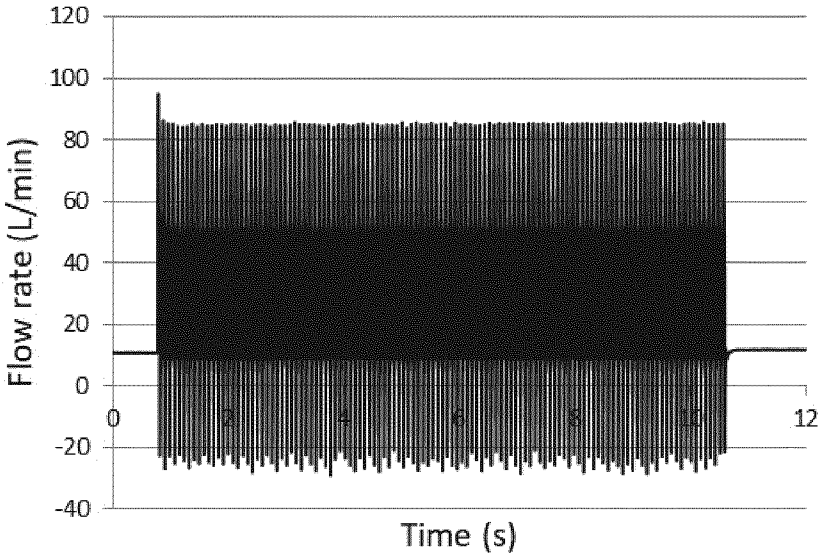


FIG. 5B

6/6

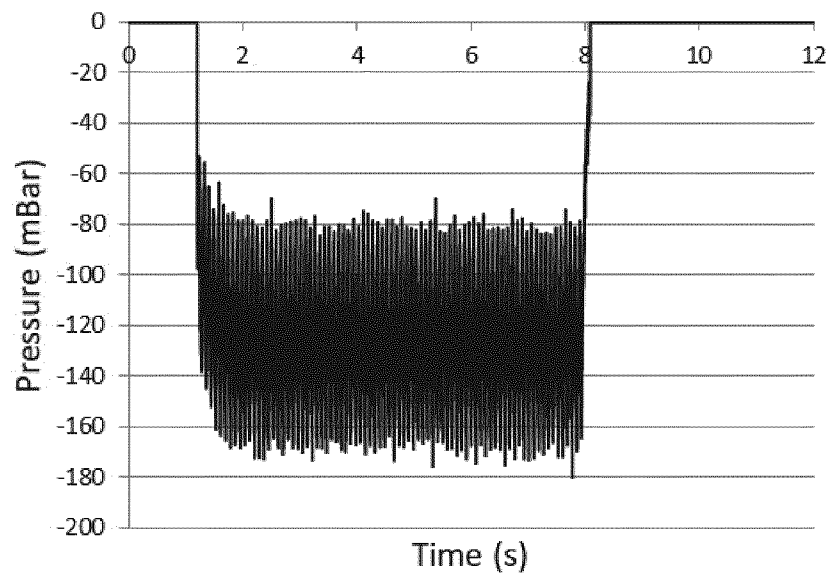


FIG. 6A

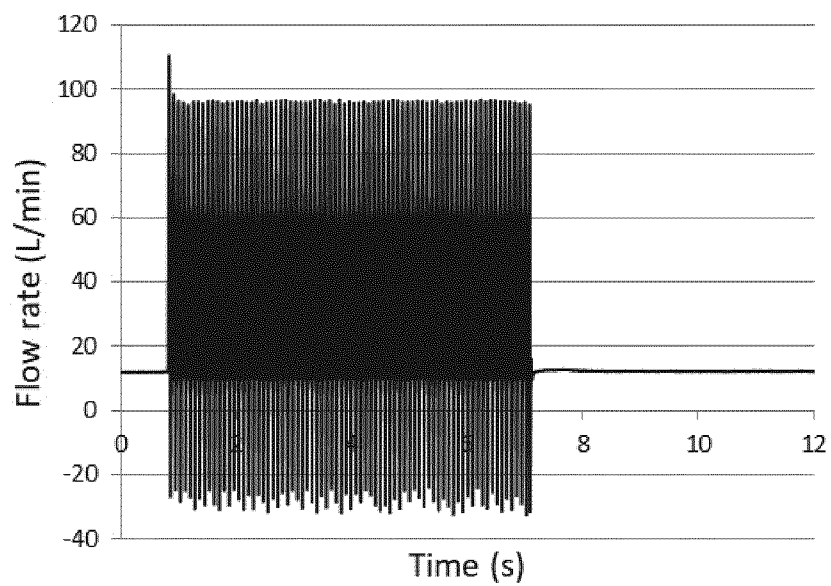


FIG. 6B

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2022/069206

A. CLASSIFICATION OF SUBJECT MATTER INV. A61M16/00 A61M16/20 ADD. A61M16/08 A61M16/04		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) A61M		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2021/008722 A1 (LOEWENSTEIN MEDICAL TECH SA [LU]) 21 January 2021 (2021-01-21) figures 1-13 page 13, paragraph 3 - page 25, paragraph 5 -----	1-9
X	US 2019/151581 A1 (GOEBEL CHRISTOF [DE]) 23 May 2019 (2019-05-23) figures 1-11 paragraph [0040] - paragraph [0100] -----	1-9
X	US 2005/051174 A1 (EMERSON GEORGE P [US]) 10 March 2005 (2005-03-10) figures 1-8 paragraph [0022] - paragraph [0026] ----- -/--	1-9
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 30 September 2022		Date of mailing of the international search report 11/10/2022
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Liess, Helmar

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2022/069206

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DE 10 2019 216553 A1 (FLO MEDIZINTECHNIK GMBH [DE]) 29 April 2021 (2021-04-29) figures 1-8 paragraph [0024] - paragraph [0044] -----	1-9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2022/069206

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **10-16**
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims;; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 10-16

Method claims 10 to 16 are directed to medical methods for treatment of the human or animal body, namely by "a method for stimulating tracheobronchial-air ... (iii) connecting said tracheobronchial-air stimulation device (1) to a subject via the physiological interface (16); (iv) applying an expiration cycle comprising a plurality of successive expirations to the subject ..." (claim 9). For this reason they relate to a subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) PCT, wherein no search and therefore no examination, Rule 66.1(e) PCT and Rule 67.1(iv), shall be required.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2022/069206

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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