DEVICE FOR THE TREATMENT OF RESPIRATORY COMPLICATIONS ARISING FROM BACTERIAL, VIRAL, AND/OR MICROBIAL INFECTIONS USING FAR-UVC IRRADIATION DELIVERED BY NEBULIZED SOLUTIONS

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PATENT DOCUMENTS U.S.

10,549,062 B2   2/2020   Murphy et al.

OTHER PUBLICATIONS

(4) “Inhalation therapy in mechanical ventilation”, Maccari et al, Sociedade Brasileira de Pneumologia, 2015; Vol 41, No. 5, pages 467-472.

ABSTRACT

This invention is a treatment for complications arising from bacterial and viral microbial infections in human lungs. The invention uses nebulized solutions to deliver far-UVC light irradiation to the deep airways within the lungs. Extended exposure to far-UVC light inactivates microorganisms which renders them non-viable. The treatment process is either controlled by a Deep Learning Neural Network or manually by a clinician. The treatment is administered by a ventilator, BPAP, or CPAP device either non-invasively through a mask or invasively through an intubation device. The nebulization solution is dense saline mixed with a bronchodilator. The far-UVC wavelengths are in the 190 to 280 nm band.
BACKGROUND OF THE INVENTION

1. Field of Invention

There exist an urgent need to eliminate microbial bacteria and viruses that infect the human lungs which creates serious respiratory complications. These infections lead to pneumonia and sometimes death due to the inability of the lungs to perform respiratory function. This invention uses passive or mechanical ventilator (MV) nebulization to deliver ultra-violet light in the 120 to 280 nm band (far-UVC) to the human lungs for the purpose of inactivating bacteria and viruses such as MRSA, H1-N1, and COVID-19 without harming keratinocytes or lung tissue. The invention is henceforth referred to as “Ultraviolet Based Nebulization” or UV-Neb.

2. Technical Background

It is well understood that ultraviolet light at 254 nm is an effective germicide for bacteria, viruses, and other pathogenic microorganisms (Chang et al [5]). The technical challenge is to apply this far-UVC light irradiation directly to the target microorganism. This invention applies the concept of projecting light in non-line of sight directions inside a bendable tube by reflecting the light using suspended solid particles. This suspended particle environment can be created by nebulization of dense saline solutions which provides an optical pathway for the far-UVC light to reach the structures of the lungs that is reached by the nebulized liquid. This invention uses this technique to deliver the far-UVC light to the bronchial and alveoli airway within the human lungs in-vivo in a non-line of sight manner. The concept of UV absorption by aerosols is well documented by Kirchstetter and Novokov[3].

Nebulization is commonly used to deliver medication to the bronchial and alveoli structures of the human lungs which is well documented by Muccari[4]. Nebulization converts a liquid into a low pressure aerosol mist, which is a colloid suspension of fine solid particles or droplets. This mist is inhaled by a patient during the respiratory process thereby reaching the bronchial and alveoli lung structures. Jet air and ultrasonic nebulization is included as components of this invention. Jet nebulizers work by connecting tubing to a compressed air source, causing air to blast at high velocities, turning the liquid into an aerosol, which is then inhaled by the patient. Ultrasonic nebulizers work by vibrating a metal plate at ultrasonic frequencies (2 to 3 Mhz) to create a mist for inhalation.
Far-UVC light in the range of 120 to 280 nm is strongly absorbed by the nucleic acids of a microorganism. Thus causing light induced damage to the DNA and RNA of a microorganism which often results from the dimerization of pyrimidine molecules. In particular, thymine (which is only found in DNA) produces cyclobutane pyrimidine dimers. When these molecules are dimerized, it becomes very difficult for the nucleic acids to replicate and if replication does occur, it often produces a defect which prevents the microorganisms from being viable. This process is referred to as microorganism inactivation.

Since the lung airways are either the primary path of entry for bacteria and viruses or the destination of life threatening complications, UV nebulization is an effective treatment for complications resulting from microorganism infections such as COVID-19. The use of far-UVC germicidal lamps has routinely been used to disinfect surfaces and materials. This invention extents this effective germicide approach to the epithelia of the lung airways

3. Background Art

Previous studies have shown that 254 nm is near optimum for germicidal effects on microorganisms. In 1878, Arthur Downes and Thomas P. Blunt published a paper describing the sterilization of bacteria exposed to ultraviolet UV light in the 250 nm to 280 nm range. At these wavelengths, UV light is mutagenic to bacteria, viruses and other microorganisms. This process is similar to the effect of UV wavelengths that produce sunburns in humans. Microorganisms have less protection from UV light and cannot survive prolonged exposure to it. In 2015 Motley and Maxey [1] reported the effectiveness of using a UV light based device to reduce infections associated with central venous, arterial, and urinary catheters. The Motley-Maxey catheter devices use ultraviolet C (UVC) and B (UVB) band light to inactivate microbial biofilm on the surface of catheters in-vivo.

Disclosures that address elimination of bacteria, viruses, fungal, and microorganism using nebulization techniques include:

U.S. PATENT 10,549,062 B2 discloses a treatment for complications arising from and/or preventing respiratory disorders caused by bacterial, viral, protozoal, fungal and/or microbial infections, preferably for treatment of complications arising from cystic fibrosis. The primary
medication in this invention is nitric oxide gas. This disclosure does not include utilization of ultraviolet light during nebulization as a treatment to inactivate microorganisms in the lungs.

**U.S. PATENT 10,588,918 B2** discloses methods for treating pulmonary infection by nebulizing a liposomal complexed aminoglycosides. The techniques used in this treatment do not include using ultraviolet light during nebulization.

**SUMMARY OF INVENTION**

This device provides a safe and effective treatment to inactivate bacterial, viral, and other microorganisms that lead to human lung infections. The treatment is delivered by using nebulized dense saline solution to provide an optical path for far-UVC irradiation of the bronchial and alveoli airways of the human lung. The far-UVC irradiation inactivates the microorganism by dimerizing the nucleic acid in the microorganism thus rendering it non-viable. The treatment is effective against MRSA, H1-N1, MERS, SARS, and COVID-19 type infections.

It is well understood that far-UVC light inactivates bacteria, viruses, and microorganisms Change et al. It is also known that strong levels of far-UVC can cause destruction of healthy tissue. The levels of far-UVC irradiation that safely provide microorganism inactivation without causing keratinocyte damage have been established by Chang et al. This invention addresses the challenge of **delivering the far-UVC irradiation in-vivo inside the human lung airways** at levels that inactivates the bacteria or virus while minimizing destruction of internal lung tissue. This balance is achieved by real-time monitoring of the state of the bacteria or virus within the lung and adjusting the irradiation intensity and irradiation on-off pulse rate to a safe level that minimizes healthy cell destruction. This balancing process is controlled by spectral analysis (SA) of the microorganism and Deep Learning Neural Networks (DLNN) Artificial Intelligence (AI).

**BRIEF DESCRIPTION OF THE DRAWINGS**

The invention is illustrated by way of example and not by way of limitation in the figures of the accompanying drawings in which like references indicate similar elements. It should be noted
that references to “an” or “one” embodiment in this disclosure are not necessarily to the same embodiment and such references mean at least one.

**Figure 1** Pulmonary System Anatomy

**Figure 2** One Embodiment of UV-Neb Invention

**Figure 3** Second Embodiment of UV-Neb Invention

**Figure 4** Third Embodiment of UV-Neb Invention

**Figure 5** Colony Survival vs Irradiation Level

**Figure 6** Example Deep Learning Neural Network Architecture

**Figure 7** Sign Activation Function

**Figure 8** ReLu Activation Function

**Figure 9** Identity Activation Function

![Bronchi, Bronchial Tree, and Lungs](image)

**Figure 1**
Figure 4

Figure 5
Figure 6

Figure 7

Figure 8

Figure 9
Where:

\( V \) - Neural Network Feature Set Inputs

\( W \) - Node Weights

\( b \) - Node Biases

\( Y \) - Hidden Layer Node Output; \( Y \) – Neural Network Output

**Equation 1**
One embodiment of the UV-Neb invention is illustrated in Figure 2. This configuration uses a positive airway source 201 (i.e. ventilator, CPAP, BPAP, etc.) to provide medium pressure breathing air 209, 203 that flows through the lungs airway structures. A flow sensor 202 is included to regulate the breathing air such that sufficient pressure is provided to push the nebulized liquid into the lungs. A fiber optics link 207 connects the far-UVC irradiation source 206 to the patient interface device 204 where its output light uses nebulized dense saline liquid as an optical path to the lung airway structures 106, 101, 102, 103, 104, 108, 107. A controller 205 is included to manage the air flow and irradiation intensity of the far-UVC light. The controller settings for the irradiation intensity, spectral characteristics, and irradiation on-off pulse rate for the far-UVC irradiation are manually set by the clinician. The nebulization process is accomplished with a nebulizing cup 211, air hose 210, and associated compressed air source 212. This configuration is a non-invasive treatment and is primarily used to treat mild pulmonary bacterial and viral infections that do not require high far-UVC irradiation levels deep into the lungs. During the nebulization and UV irradiation process, bronchodilators such as albuterol, levalbuterol, and epinephrine injection are used to dilate the smooth muscles within the airways to provide maximum irradiation exposure. The patient interface device 204 is a standard mask used with ventilators, CPAP, and BPAP devices with an entry for the distal tip of a fiber-optic cable 207.

A second embodiment of the UV-Neb invention is illustrated in Figure 3. This configuration uses a positive airway source 302 (i.e. ventilator, CPAP, BPAP, etc.) to provide medium pressure breathing air 301, 304 that flows through the lungs airway structures. A flow sensor 303 is included to regulate the breathing air such that sufficient pressure is provided to push the nebulized liquid into the lungs. The patient interface device is an intubation tube 308 augmented with entry points for a fiber-optic cable 306 that is routed through the intubation tube deep into the trachea reaching the trachea divide to deliver far-UVC irradiation to the primary bronchi. The intubation device also includes entry for the positive air flow 304 and the nebulized mist cup 311 output. The nebulization process is accomplished with a jet or ultrasonic nebulizing cup 311, air hose 312, and associated compressed air source 310. This configuration is an invasive treatment and is used to treat severe pulmonary bacterial and viral infections where intubation and breathing assistance is required. During the nebulization and UV irradiation process,
bronchodilators such as albuterol, levalbuterol, and epinephrine injection are used to dilate the smooth muscles within the airways to provide maximum irradiation exposure. In this configuration, the controller settings for the irradiation intensity, spectral wavelength, and irradiation on-off pulse rate for the far-UVC irradiation are manually set by the clinician. Irradiation energy levels are predetermined in a laboratory environment, thus ensuring minimum keratinocyte and lung tissue damage.

A third embodiment of the UV-Neb invention is illustrated in Figure 4. This configuration is the complete utilization of all components of the invention. A positive airway source 402 (i.e. ventilator, CPAP, BPAP, etc.) provides medium pressure breathing air 401, 404 that flows through the lungs airway structures. A flow sensor 403 is included to regulate the breathing air such that sufficient pressure is provided to push the nebulized liquid into the lungs. An ultrasonic nebulization cup 411 and associated air compressor provides the entry of the aerosol mist into the airway flow through the intubation device 408. The patient 409 interface device is an intubation tube 408 augmented with entry points for a fiber-optic cable 406 that is routed through the intubation tube into the trachea reaching the trachea divide to deliver far-UVC irradiation to the primary bronchi. A far-UVC irradiation source 407 capable of wavelengths in the 120 to 625 nm bands at levels of 0 to 20 mj/cm² is included to irradiate and fluoresce the target microorganism. A 190 to 1100 nm spectrometer 413 is included for analysis of the fluoresced microorganism to detect the spectral signature and density of the infection present in the lung airways. The spectrometer includes a miniature sensor that is inserted in the trachea through the intubation device 408.

The controller 405 used is this configuration automatically sets the irradiation wavelength (120 to 280 nm), irradiation level (0 to 20 mj/cm² ) 501, positive breathing air flow rate (10 to 40 cmH₂O), and ultrasonic nebulizer frequency (1.8 to 3.0 MHz). The controller also reads the spectral analysis data from the fluoresced microorganism by the 190 to 1100 nm spectrometer which in conjunction with the AI Deep Learning Network measures the efficacy of the irradiation protocol set by the controller 405. This process is designed to maintain a balance between irradiation levels that destroy the bacteria or virial colony while staying below a level that destroys keratinocytes and/or healthy lung tissue. The AI algorithms maintain this balance. The irradiation exposure time required to inactivate the microorganism is dependent on the irradiation level. The bacteria or virus spectral pattern indicates when the microorganism is
inactive and no longer requires irradiation. This decision can be determined automatically by the AI algorithms executed in the controller or manually by the clinician.

The basic neural network architecture used in the UV-Neb invention is illustrated in Figure 6 and is provided as a shallow network for sake of explanation. In the full utilization of all components of this invention, a Deep Learning Neural Network is used to maintain the irradiation balance that minimizes far-UVC damage to lung tissue. The neural network’s input feature set 601 comes from the spectrometer that is inserted in the trachea while being irradiated with wavelengths that fluoresces the bacteria or viral microorganism. This spectrometer data is the unique spectral patterns associated with the type and state of the microorganisms. Each node input corresponds to a spectrum wavelength window energy level (i.e. wavelength, magnitude). An active microorganism has a unique spectral pattern based on its type and infection density. As the microorganism is inactivated, its spectral pattern changes 502, (i.e. decrease in density, spectral shift) which is an indication of the effectiveness of the far-UVC irradiation.

The architecture of the neural network consist of hidden layers with multiple nodes 602, 603, 604 that are used to learn the weights and their associated biases 606, 607, 608. The hidden layers use a ReLu Activation Function 801 and the output level uses a Sign Activation Function 701. The input level uses an Identity Activation Function 901. The loss function is least squares regression whose results are used for backpropagation during training.

This invention’s Neural Network training data is derived from the spectral patterns of specific microorganisms in a laboratory environment. The Neural Network can be retrained for any microorganism spectral pattern of interest and therefore allows the creation of weighting and biases for multiple types of microorganisms. The particular target bacteria or virus is selectable by the clinician.

The neural network output nodes indicate the spectrum and density levels of each detected microorganism type. This data is used to automatically set the irradiation level on a real-time basis. The AI neural network process is equivalent to observing the microorganism microscopically and making a cognitive decision on the type and infection level of the microorganism. The mathematical relationship describing the three hidden layer shallow neural network shown in Figure 6 is given by Equation 1. A detail description of this process is provided by A. Pandya and R. Macy[6].
CLAIMS

We Claim:

1. A method for the treatment of respiratory disorders caused by bacterial, viral, and/or microbial infections in a human lung; said method comprising:
An apparatus containing a positive air source augmented with a nebulizer, far-UVC light source, UV spectral analyzer, and an AI based controller. The apparatus components include:

- a positive airway pressure device for providing breathing gas to a patient interface;
- a air flow sensor and control valve for sensing and regulating breathing air flow rate;
- a far-UVC irradiation source for inactivating the microorganism nucleus;
- a UV fluorescence source used to identify spectrum of the in lung microorganism;
- a UV spectrometer for analyzing the spectral content and density of the fluoresced microorganism;
- a ultrasonic nebulizer source for creating a nebulized mist;
- a nebulizer air compressor source for creating a nebulized mist;
- a patient invasive or non-invasive device for dispensing nebulized liquids to airways;
- a nebulizer liquid dispenser cup dense saline and bronchodilator liquids;
- a fiber optics far-UV delivery cable to deliver irradiation energy within lungs; and
- a controller that automatically or under clinician control set the operation parameters of the UV Nebulizer system.

2. The method of Claim 1, wherein a non-invasive patient interface device is used, a manual controller sets the far-UVC wavelength and the irradiation on-off cycle, ultrasonic or jet air nebulization is used, and there is no AI spectral processor or UV spectrometer.

3. The method of Claim 1, wherein an invasive intubation patient interface device is used, a manual controller sets the far-UVC wavelength and the irradiation on-off cycle, ultrasonic or jet air nebulization is used, and there is no AI spectral processor or UV spectrometer.

4. The method of Claim 1, wherein an invasive intubation patient interface device is used, a Deep Learning Neural Network directed controller sets the far-UVC wavelength and
the irradiation on-off cycle, ultrasonic nebulization is used, and a UV spectrometer provides the input feature set.

5. The method of Claim 4, wherein training data for the associated Neural Network is derived in a laboratory environment for each specific microorganism type.

6. The method of Claim 4, wherein the fluoresced microorganism’s spectral pattern is used to detect its presence.

7. The method of Claim 1, wherein a fiber-optic cable delivering the far-UVC irradiation is inserted in the nasal sinus of the patient.

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