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Office de la Propriété Intellectuelle du Canada

Innovation, Science and Economic Development Canada
Canadian Intellectual Property Office

CA 3218826 A1 2022/11/17

(21) 3 218 826

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) **Date de dépôt PCT/PCT Filing Date:** 2022/05/09
(87) **Date publication PCT/PCT Publication Date:** 2022/11/17
(85) **Entrée phase nationale/National Entry:** 2023/11/10
(86) **N° demande PCT/PCT Application No.:** US 2022/028332
(87) **N° publication PCT/PCT Publication No.:** 2022/240747
(30) **Priorité/Priority:** 2021/05/10 (US63/186,318)

(51) **Cl.Int./Int.Cl.** ***A61B 5/0205*** (2006.01), ***A61B 5/0245*** (2006.01), ***A61B 5/05*** (2021.01), ***A61B 5/08*** (2006.01)

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(54) **Titre : SYSTEME ET PROCEDE DE QUANTIFICATION DE LA RESPIRATION**
(54) **Title: SYSTEM AND METHOD FOR QUANTIFICATION OF RESPIRATION**

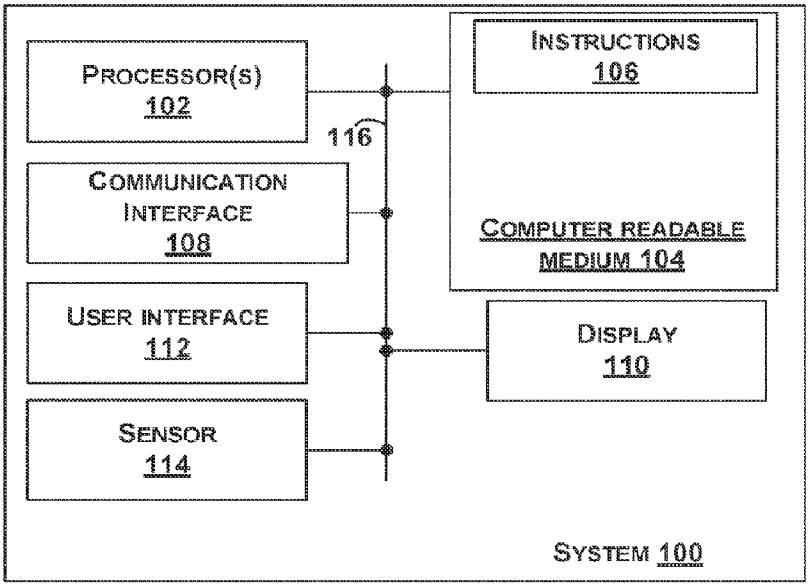

FIG. 1

(57) **Abrégé/Abstract:**
A system includes one or more processors, a user interface, a. sensor, and a. computer readable medium storing instructions that, when executed by the one or more processors, cause the system to perform functions. The functions include generating, via the sensor, a signal representing vibrations originating from a. blood vessel of a patient and generating an intensity' spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations. The functions also include identifying a first peak of the intensity spectrum that corresponds to a respiratory' frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient. The functions also include performing a comparison of a. first intensity of the first peak with a second intensify of the second peak and generating, via the user interface, output indicative of the comparison.

Date Submitted: 2023/11/10

CA App. No.: 3218826

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A system includes one or more processors, a user interface, a. sensor, and a. computer readable medium storing instructions that, when executed by the one or more processors, cause the system to perform functions. The functions include generating, via the sensor, a signal representing vibrations originating from a. blood vessel of a patient and generating an intensity' spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations. The functions also include identifying a first peak of the intensity spectrum that corresponds to a respiratory' frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient. The functions also include performing a comparison of a. first intensity of the first peak with a second intensify of the second peak and generating, via the user interface, output indicative of the comparison.

SYSTEM AND METHOD FOR QUANTIFICATION OF RESPIRATION

CROSS REFERENCE TO RELATED APPLICATION

[0001] The present application is an international application claiming priority to U.S. provisional application no. 63/186,318, filed May 10, 2021, the contents of which are hereby incorporated by reference.

[0002] The following document is also hereby incorporated by reference: Respiratory Non-Invasive Venous Waveform Analysis for Assessment of Respiratory Distress in Coronavirus Disease 2019 Patients: An Observational Study, Alvis, Bret MD; Vaughn, Lexie MD; Schmeckpeper, Jeffrey MD, PhD; Huston, Jessica MD; Case, Marisa RN; Semler, Matthew MD; Lindenfeld, JoAnn MD; Brophy, Colleen MD; Hocking, Kyle PhD, doi: 10.1097/CCE.0000000000000539.

FEDERAL FUNDING STATEMENT

[0003] This invention was made with government support under Grant No. BA-R01HL148244-01 and Grant No. KH-R44HL140669-01, awarded by the National Institutes of Health. The government has certain rights in the invention.

BACKGROUND

[0004] The novel coronavirus (SARS-CoV-2) has produced a global pandemic that continues to affect both economies and healthcare systems. Although most patients with SARS-CoV-2 experience only mild symptoms, a subset of infected patients will experience life-threatening respiratory failure. Evaluation and management of respiratory distress due to COVID-19 and other causes depends on the severity of the disease. Unfortunately, knowing whose symptoms will remain mild and who will progress to severe respiratory failure is difficult, and often requires observation in a hospital setting. Rapid and effective triage can be critical for early treatment and effective allocation of hospital resources.

SUMMARY

[0005] A first aspect of the disclosure is a system comprising: one or more processors; a user interface; a sensor; and a computer readable medium storing instructions that, when executed by the one or more processors, cause the system to perform functions comprising: generating, via the sensor, a signal representing vibrations originating from a blood vessel of a patient; generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations; identifying a first peak of

the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient; performing a comparison of a first intensity of the first peak with a second intensity of the second peak; and generating, via the user interface, output indicative of the comparison.

[0006] A second aspect of the disclosure is a method comprising: generating, via the sensor, a signal representing vibrations originating from a blood vessel of a patient; generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations; identifying a first peak of the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient; performing a comparison of a first intensity of the first peak with a second intensity of the second peak; and generating, via the user interface, output indicative of the comparison.

[0007] A third aspect of the disclosure is a non-transitory computer readable medium storing instructions that, when executed by the system, cause the system to perform functions comprising: generating, via the sensor, a signal representing vibrations originating from a blood vessel of a patient; generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations; identifying a first peak of the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient; performing a comparison of a first intensity of the first peak with a second intensity of the second peak; and generating, via the user interface, output indicative of the comparison.

[0008] By the term "about" or "substantially" with reference to amounts or measurement values described herein, it is meant that the recited characteristic, parameter, or value need not be achieved exactly, but that deviations or variations, including for example, tolerances, measurement error, measurement accuracy limitations and other factors known to those of skill in the art, may occur in amounts that do not preclude the effect the characteristic was intended to provide.

[0009] The features, functions, and advantages that have been discussed can be achieved independently in various examples or may be combined in yet other examples further details of which can be seen with reference to the following description and drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] Figure 1 is a block diagram of a system, according to an example.

[0011] Figure 2 is a front view of a system, according to an example.

[0012] Figure 3 is a block diagram of a method, according to an example.

[0013] Figure 4 shows intensity spectra of vibrations originating from a patient's blood vessel, according to an example.

[0014] Figure 5 shows relationships between a calculated metric and hospitalization status and COVID-19 status, according to an example.

[0015] Figure 6 shows relationships of respiratory rate and oxygen saturation with hospitalization status and COVID-19 status, according to an example.

[0016] Figure 7 shows relationships of a calculated metric with lung disease, according to an example.

[0017] Figure 8 shows the predictive ability of a calculated metric, according to an example.

DETAILED DESCRIPTION

[0018] The present disclosure relates generally to a system used (e.g., by a physician, a nurse, or another user) to determine the level of respiratory strain and/or distress that is occurring in a patient through measurement of the peripheral venous waveform via an external sensor. This measurement system and method are applicable to respiratory conditions and diseases that are both chronic and acute, including but not limited to: viral pneumonia, bacterial pneumonia, waning from mechanical ventilation, diseases requiring oxygen support therapy, sleep apnea, asthma, COPD, restrictive pulmonary diseases, obstructive pulmonary diseases, pneumonia, allergens, medicinal overdoses/side-effects, airway obstruction, pulmonary edema, cerebral vascular accidents, spinal cord injuries, opioid overdose/misuse, inhalational injuries, Guillain-barre syndrome, myasthenia gravis, amyotrophic lateral sclerosis (ALS), cystic fibrosis, trauma, sepsis, fibrotic/restrictive respiratory diseases, and/or autonomic function related diseases.

[0019] Non-Invasive Venous waveform Analysis (NIVA) is a promising monitoring approach for assessing vascular volume states in both adults and children. NIVA typically includes the use of a piezoelectric sensor on the volar aspect of the wrist to capture a venous waveform signal. The signal is then deconvoluted into two components with a fast Fourier Transformation into the frequency domain. The cardiac component (f0) and harmonics of the cardiac component are used to derive a value that is representative of the pulmonary capillary wedge pressure (PCWP), the most common data point for volume assessment.

[0020] Signals were collected from COVID-19 patients to assess volume status and the

need for invasive measurements. Post hoc analysis was used to analyze and evaluate the respiratory component (fR0) of the venous waveform and the relationship of the respiratory component to the need for oxygen support therapy. Use of the respiratory component of the venous waveform can provide a rapid, non-invasive, inexpensive test to identify patients with COVID-19 at risk for requiring oxygen therapy.

[0021] The disclosure will now be described more fully hereinafter with reference to the accompanying drawings, in which exemplary embodiments of the disclosure are shown. This disclosure may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein. Rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the disclosure to those skilled in the art. Like reference numerals refer to like elements throughout.

[0022] Figure 1 is a block diagram of a system 100. The system 100 includes one or more processors 102, a non-transitory computer readable medium 104 storing instructions 106, a communication interface 108, a display 110, a user interface 112, and a sensor 114. Components of the system 100 are linked together by a system bus, network, or other connection mechanism 116.

[0023] The one or more processors 102 can be any type of processor(s), such as a microprocessor, a digital signal processor, a multicore processor, etc., coupled to the non-transitory computer readable medium 104.

[0024] The non-transitory computer readable medium 104 can be any type of memory, such as volatile memory like random access memory (RAM), dynamic random access memory (DRAM), static random access memory (SRAM), or non-volatile memory like read-only memory (ROM), flash memory, magnetic or optical disks, or compact-disc read-only memory (CD-ROM), among other devices used to store data or programs on a temporary or permanent basis.

[0025] Additionally, the non-transitory computer readable medium 104 stores instructions 106. The instructions 106 are executable by the one or more processors 102 to cause the system 100 to perform any of the functions or methods described herein.

[0026] The communication interface 108 includes hardware to enable communication within the system 100 and/or between the system 100 and one or more other devices. The hardware can include transmitters, receivers, and antennas, for example. The communication interface 108 can be configured to facilitate communication with one or more other devices, in accordance with one or more wired or wireless communication protocols. For example, the

communication interface 108 can be configured to facilitate wireless data communication for the system 100 according to one or more wireless communication standards, such as one or more Institute of Electrical and Electronics Engineers (IEEE) 801.11 standards, ZigBee standards, Bluetooth standards, etc. As another example, the communication interface 108 can be configured to facilitate wired data communication with one or more other devices.

[0027] The display 110 can be any type of display component configured to display data. As one example, the display 110 can include a touchscreen display. As another example, the display 110 can include a flat-panel display, such as a liquid-crystal display (LCD) or a light-emitting diode (LED) display.

[0028] The user interface 112 can include one or more pieces of hardware used to provide data and control signals to the system 100. For instance, the user interface 112 can include a mouse or a pointing device, a keyboard or a keypad, a microphone, a touchpad, or a touchscreen, among other possible types of user input devices. Generally, the user interface 112 can enable an operator to interact with a graphical user interface (GUI) provided by the system 100 (e.g., displayed by the display 110).

[0029] The sensor 114 generally takes the form of a piezioelectric sensor, an optical sensor, a multiplexed optical array, a pressure sensor, a force resistive sensor, a tonometer, an ultrasound sensor, a capacitive sensor, or a pressure transducer. For example, the sensor 114 can be a piezioelectric sensor that communicates wirelessly or via a wired connection with the one or more processors 102. Additionally or alternatively, the sensor 114 is securable to a skin of a patient via a strap and/or encapsulated within rubber, a polymer, polyurea, and/or silicone.

[0030] Figure 2 is a front view of the system 100. As shown, the system 100 includes the sensor 114 that communicates via a wired connection with the one or more processors 102 (not shown). Also shown in Figure 2 are the user interface 112 and the display 110.

[0031] Figure 3 is a block diagram of a method 300. As shown in Figure 3, the method 300 includes one or more operations, functions, or actions as illustrated by blocks 302, 304, 306, 308, and 310. Although the blocks are illustrated in a sequential order, these blocks may also be performed in parallel, and/or in a different order than those described herein. Also, the various blocks may be combined into fewer blocks, divided into additional blocks, and/or removed based upon the desired implementation.

[0032] At block 302, the method 300 includes the system 100 generating, via the sensor 114, a signal representing vibrations originating from a blood vessel of a patient. In various examples, the blood vessel is a peripheral vein or a peripheral artery. The vibrations generally

include vibrations generated by blood flowing against walls of the blood vessel or vibrations that are inherently present when a fluid like blood is flowing through a conduit like a blood vessel. Pulsatile flow is a result of forward moving blood from the arterial side as well as blood being pulled by the right side of the heart through the venous system. When the sensor 114 is a piezoelectric sensor, for example, the signal can represent displacement of the sensor 114 caused by the vibrations with respect to time. The signal generated by the sensor 114 can represent the vibrations that are generated via retrograde transmission of a negative pressure exerted on the patient's venous system by inspiratory pressures.

[0033] Typically, the sensor 114 is pressed against the patient's skin (*e.g.*, with a back pressure of 10 mmHg to 60 mmHg) with a strap, microneedles, suction negative pressure or another restraint or attachment device while the system 100 generates the signal. In various examples, the sensor 114 is pressed against the skin at the wrist, the ankle, the eye, or the neck. In other examples, the sensor 114 is inserted into the ear canal.

[0034] At block 304, the method 300 includes the system 100 generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations. The system 100 generally generates the intensity spectrum by performing a Fourier transform (*e.g.*, a fast Fourier transform (FFT)) upon the signal. Figure 4 shows three examples of an intensity spectrum.

[0035] Figure 4 shows representative signals from patients with low risk to high risk of O_2 support need (left to right). Raw signals are transformed from the time domain (top) to the frequency domain (bottom). The relative amplitude of the respiratory rate (f_{R0}, fundamental frequency) compared to the relative amplitude of the pulse rate (f_0) is used to calculate a RIVA Respiratory Index (RIVA-RI). RIVA-RI is calculated based on the ratio of the relative amplitude of f_{R0} and f_0: RIVA-RI=f_{R0}/f_0

[0036] Panel A of Figure 4 represents a healthy control patient. Three easily recognizable peaks are shown at approximately 1.4 Hz (f_0), 2.8 Hz, and 4.2 Hz. The peak at 1.4 Hz (f_0) is the fundamental frequency or first harmonic of the patient's heartbeat, the peak at 2.8 Hz is the second harmonic of the patient's heartbeat, and the peak at 4.2 Hz is the third harmonic of the patient's heartbeat. There is a small peak at about 0.5 Hz that is the fundamental frequency or first harmonic of the patient's breathing rate (f_{R0}).

[0037] Panel B of Figure 4 represents a COVID positive patient with no need for supplemental oxygen treatment. Three easily recognizable peaks are shown at approximately at 1.4 Hz (f_0), 2.8 Hz, and 4.2 Hz. The peak at 1.4 Hz (f_0) is the fundamental frequency or first harmonic of the patient's heartbeat, the peak at 2.8 Hz is the second harmonic of the

patient's heartbeat, and the peak at 4.2 Hz is the third harmonic of the patient's heartbeat. There is a small peak at about 0.5 Hz that is the fundamental frequency or first harmonic of the patient's breathing rate (f_{R0}).

[0038] Panel C of Figure 4 represents a COVID positive patient with a need for supplemental oxygen treatment. Two easily recognizable heartbeat peaks are shown at approximately at 1.8 Hz (f_0) and 3.6 Hz. The peak at 1.8 Hz (f_0) is the fundamental frequency or first harmonic of the patient's heartbeat and the peak at 3.6 Hz is the second harmonic of the patient's heartbeat. There is a large peak at about 0.5 Hz that is the fundamental frequency or first harmonic of the patient's breathing rate (f_{R0}).

[0039] At block 306, the method 300 includes the system 100 identifying a first peak of the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient.

[0040] Referring to panel A, panel B, and panel C of Figure 4, the system 100 identifies the first peak that corresponds to the respiratory frequency (f_{R0}) (*e.g.*, the fundamental respiratory frequency) of the patient and the second peak that corresponds to a heart rate (f_0) (*e.g.*, the fundamental heart beat frequency) of the patient. The system 100 identifies the first peak and the second peak automatically or manually.

[0041] For example, the system 100 can automatically identify the first peak (f_{R0}) as being a most intense peak of any peaks within a range of 0.1 Hz to 0.5 Hz, which is a range within which the fundamental respiratory frequency would be expected to be. In some cases, the patient's respiratory rate can be somewhat irregular, leading to a broader but less intense peak that corresponds to a range of frequencies instead of a singular frequency. As such, the system 100 can identify the first peak (f_{R0}) by determining that the first peak (f_{R0}) represents a greatest amount of energy (*e.g.*, area under the curve of the intensity spectrum) of any peaks within the range of 0.1 Hz to 0.5 Hz.

[0042] Likewise, the system 100 can automatically identify the second peak (f_0) as being a most intense peak of any peaks within a range of 0.5 Hz to 3.5 Hz, which is a range within which the fundamental heart beat frequency would be expected to be. In some cases, the patient's heart rate can be somewhat irregular, leading to a broader but less intense peak that corresponds to a range of frequencies instead of a singular frequency. As such, the system 100 can identify the second peak (f_0) by determining that the second peak (f_0) represents a greatest amount of energy (*e.g.*, area under the curve of the intensity spectrum) of any peaks within the range of 0.5 Hz to 3.5 Hz.

[0043] In some examples, the system 100 receives, via the user interface 112, an input

explicitly identifying the first peak (f_{RO}) as corresponding to the fundamental respiratory frequency. More specifically, the user could identify the first peak (f_{RO}) using a touch screen gesture. In this context, the system 100 identifies the first peak (f_{RO}) based on the input received via the user interface 112.

[0044] Likewise, the system 100 receives, via the user interface 112, an input explicitly identifying the second peak (f_0) as corresponding to the fundamental heart beat frequency. More specifically, the user could identify the second peak (f_0) using a touch screen gesture. In this context, the system 100 identifies the second peak (f_0) based on the input received via the user interface 112.

[0045] In yet other examples, the system 100 receives an input from an additional sensor such as a pneumograph, with the input identifying the first peak (f_{RO}). As such, the system 100 identifies the first peak (f_{RO}) based on the received input. That is, the input received from the additional sensor explicitly indicates the respiratory rate and the system 100 identifies the first peak (f_{RO}) based on the respiratory rate indicated by the received input.

[0046] Likewise, the system 100 receives an input from an additional sensor such as a pulse sensor, with the input identifying the second peak (f_0). As such, the system 100 identifies the second peak (f_0) based on the received input. That is, the input received from the additional sensor explicitly indicates the heart rate and the system 100 identifies the second peak (f_0) based on the heart rate indicated by the received input.

[0047] At block 308, the method 300 includes the system 100 performing a comparison of a first intensity of the first peak with a second intensity of the second peak. For example, the system 100 calculates a ratio of the first intensity of the first peak (f_{RO}) to the second intensity of the second peak (f_0) or a ratio of the second intensity of the second peak (f_0) to the first intensity of the first peak (f_{RO}).

[0048] The greater the ratio of the first intensity of the first peak (f_{RO}) to the second intensity of the second peak (f_0), the more likely it is that the patient needs or will need supplemental oxygen therapy.

[0049] At block 310, the method 300 includes the system 100 generating, via the user interface 112, output indicative of the comparison (*e.g.*, the ratio of the first intensity of the first peak (f_{RO}) to the second intensity of the second peak (f_0) or the ratio of the second intensity of the second peak (f_0) to the first intensity of the first peak (f_{RO})).

[0050] In various examples, the system 100 uses a table or an equation that maps values of the ratio to values of various health (*e.g.*, respiratory) metrics. For example, data could be collected experimentally, with the data indicating how various health metrics correlate with

the ratio discussed above. Statistical techniques can be used to define mathematical functions that define the relationship between each of the health metrics and the calculated ratio. As such, the system 100 can produce output that indicates the values of various metrics based on the calculated ratio.

[0051] For example, the output can indicate one or more of: a diffusing capacity of the patient's lung for carbon monoxide (DLCO), a diffusing capacity of the patient's lung for carbon monoxide divided by an alveolar volume (DLCO/VA), an inspiratory reserve volume (IRV) for the patient's lung, a maximum rate of oxygen consumption (VO_2 max), a work of breathing, a pleural pressure, or an inspiratory capacity (IC) for the patient's lung. As such, prior to generating the output, the system can determine, based on the comparison of the first intensity corresponding to the respiratory frequency and the second intensity corresponding to the heart rate, one or more of the DLCO, DLCO/VA, IRV, the VO_2 max, the work of breathing, the pleural pressure, or the IC, and generate the output accordingly.

[0052] In spontaneous breathing, the components of the work of breathing include: 1) work needed by the muscles of respiration to overcome elastic recoil of the lung and to displace the chest wall and abdomen, 2) the work needed to overcome airway resistance and lung viscosity, and 3) work needed to overcome inertia. Increased work of breathing is believed to be correlated with an increased ratio of the first intensity corresponding to the respiratory rate over the second intensity corresponding to the heart rate.

[0053] Treatment or therapy for the patient can be initiated, adjusted, or ceased based on the results of the comparison, *i.e.*, the outputs generated by the system 100. For example, a dosage, frequency, or duration of a supplemental oxygen treatment and/or a continuous positive airway pressure (CPAP) treatment for the patient can be altered based on the output of the system 100.

[0054] In various examples, the patient is experiencing a pulmonary disease such as chronic obstructive pulmonary disease (COPD), sleep apnea, bronchiectasis, asthma, pulmonary edema, congestion, pneumothorax, pneumonia, allergens, medicinal overdoses/side-effects, airway obstruction, pulmonary edema, cerebral vascular accidents, spinal cord injuries, opioid overdose/misuse, inhalational injuries, Guillain-barre syndrome, myasthenia gravis, amyotrophic lateral sclerosis (ALS), cystic fibrosis, sepsis, respiratory distress, acute respiratory distress syndrome, idiopathic pulmonary fibrosis, or pulmonary fibrosis, and the corresponding treatment can be informed by the results of the comparison

[0055] The ratio (RIVA-RI) of the first intensity corresponding to the respiratory rate over the second intensity corresponding to the heart rate being greater than 0.6 yielded a 92%

sensitivity (95% CI, 61.52% to 99.79%) and 47% specificity (95% CI, 28.34% to 65.67%) in predicting a COVID-19+ patient's future need for oxygen support therapy.

[0056] Healthy control patients displayed significantly lower RIVA-RI values compared to patients with idiopathic pulmonary fibrosis.

[0057] When each adult (N=4, Ages= 38 years, 34 years, 22 years, and 21 years) reached their VO_2 max, RIVA-RI increased from a median baseline of 0.03 to a value of 0.78 suggesting that RIVA-RI increases relative to increasing oxygen demand.

[0058] Data collected from patients experiencing respiratory distress, defined by the need for oxygen support therapy, demonstrated a significant elevation in the respiratory venous waveform amplitude in relation to the cardiac venous waveform amplitude, that is, an increase in RIVA-RI.

[0059] Data from the preliminary observational study suggests that a RIVA-RI value of greater than or equal to 0.6 had an AUC=0.64 with a sensitivity of 92% and specificity of 47% in predicting a COVID-19+ patients' future need for oxygen support therapy.

[0060] **ADDITIONAL EXAMPLES**

[0061] The coronavirus 2 (SARS-CoV-2) has led to a global pandemic that has crippled both economies and healthcare. The coronavirus pandemic highlighted the lack of innovation in respiratory monitoring. There is currently no non-invasive monitor available to obtain respiratory physiologic information except traditional spirometry, pulse oximetry, and various ways of counting respiration rates. These technologies have been around for decades. This pandemic proved more is necessary to adequately monitor and triage patients experiencing acute respiratory distress. One of the major issues with respiratory disease is it can quickly propagate to life-threatening respiratory failure. Whether it by COVID-19, traditional viral/bacterial pneumonia, asthma, and/or any other acute on chronic pulmonary disease, patients with mild symptoms typically can recover from home and not further burden the healthcare system. Unfortunately, knowing whose symptoms will remain mild and who will acutely progress to severe respiratory failure is difficult and, often requires observation in a hospital setting. The sudden deterioration of respiratory insufficiency to failure remains a major concern and often results in liberal hospital triage. The unique characteristics of respiratory disease and the vast caseload that can exist in a viral pandemic that primarily effects the pulmonary system, suggest that rapid and effective triage are critical for early treatment and effective allocation of hospital resources.

[0062] Peripheral venous waveforms can be captured non-invasively at the wrist using a piezo-electric sensor. These are low amplitude waveforms that typically require signal

processing and amplification for analysis. The Fourier transformation can then be used to bundle windows of waveforms and present the data in the frequency (instead of time) domain. This leads to a low amplitude waveform at approximately 0.2 Hz (termed "f_{R0}") that corresponds to respiration (equivalent to 12 breaths/minute). This wave is likely due to retrograde propagation of the negative intrathoracic pressure during inspiration from the right atrium/vena cava, throughout the venous system. There is an additional peak waveform at about 1 Hz equivalent to the cardiac frequency. This signal and harmonics of the fundamental cardiac frequency have been used to develop an algorithm that allows for the evaluation of volume status.

[0063] The weighted contributions of the amplitudes of the respiratory signal (f_{R0}) can be ratiometrically normalized to amplitude of the frequency of the pulse rate (f_0) to produce a Respiratory non-Invasive Venous waveform Analysis – respiratory index (RIVA-RI). Fifty COVID-19+ patients that required oxygen support therapy were compared to COVID-19+ patients that did not require oxygen support, as shown in Figure 5.

[0064] The RIVA-RI for COVID-19 positive patients (COVID-19+) admitted to the hospital and requiring oxygen support during hospitalization (median = 0.27, n = 34) was higher ($p < 0.01$, 95% CI 0.4008 – 2.037) than the RIVA-RI for COVID-19 negative controls (median = 0.06, n = 34). The RIVA-RI for COVID-19 + patients that required oxygen support was also higher ($p = 0.02$, 95% CI 0.1023 – 1.939) than the RIVA-RI for those same patients at time of discharge (median = 0.12, n = 24). The RIVA-RI was not different ($p = 0.09$, 95% CI -0.1242 – 2.265) for COVID-19+ patients that required oxygen support during hospitalization and those COVID-19+ patients that never required oxygen support during hospitalization (median = 0.2, n = 11). Statistical analysis was completed with multiple comparisons between groups. Horizontal bars with star (*) demonstrate statistical significance. The ability of the RIVA-RI for predicting the need for oxygen support (B) during admission for COVID-19 positive patients demonstrated an AUC of 0.64 (95% CI, 0.48– 0.81). At a RIVA-RI value of ≥ 0.6, the result was a 92% sensitivity (95% CI, 61.52% to 99.79%) and 47% specificity (95% CI, 28.34% to 65.67%) for predicting need for oxygen support during admission for COVID-19 positive patients. The above abbreviations are defined as follows: COVID 19+ = positive for the SARS-CoV-2 virus; COVID-19- = negative for the SARS-CoV-2 virus; O_2 = oxygen; RIVA-RI= Respiratory non-Invasive Venous waveform Analysis – Respiratory Index; AUC= area under the curve.

[0065] Patients that required oxygen support therapy had a significantly higher ($p=0.02$, 95% CI 0.1023 – 1.039) median RIVA-RI (median=0.6, n=34) compared to discharge RIVA-

RI (median= 0.12, n=24) and significantly higher ($p<0.01$, 95% CI 0.4008-2.037) than the median RIVA-RI of healthy controls (median=0.06, n=34) (Figure 3). The ability of RIVA-RI to predict the need for oxygen support therapy during admission for COVID-19+ patients demonstrated an AUC=0.64 (95% CI, 0.48-0.81). A key point on the ROC curve demonstrated that a RIVA-RI value of ≥ 0.6 had a 92% sensitivity (95% CI, 61.52% to 99.79%) and 47% specificity (95% CI, 28.34% to 65.67%) in predicting a COVID-19+ patients' future need for oxygen support therapy. Neither respiratory rate (RR) nor oxygen saturation determined with pulse oximetry (SpO_2) demonstrated any relationship to oxygen support therapy needs in COVID-19 patients in this study, as shown in Figure 6.

[0066] There was no significant difference ($p = 0.13$, 95% CI -0.7309 – 8.28) in the respiratory rate (A) between COVID-19 positive patients (COVID-19+) requiring oxygen support during hospitalization ($n = 34$) and those without oxygen support during hospitalization ($n = 11$) or between COVID-19 positive patients on admission to the hospital ($n = 34$) and at discharge ($n = 27$; $p = 0.66$, 95% CI -1.944 – 4.974). COVID-19+ patients that required oxygen support during hospitalization had a significantly lower oxygen saturation (B, SpO_2) on admission ($n = 34$; $p < 0.01$, 95% CI 2.536 – 8.727) and at discharge ($n = 27$; $p < 0.01$, 95% CI 0.8066 – 7.426) than COVID-19 positive patients that did not require oxygen support during hospitalization ($n = 12$). Statistical analysis was completed with multiple comparisons between groups. Horizontal bars with star (*) demonstrate statistical significance.

[0067] An additional proof of concept study was performed in patients with chronic pulmonary conditions that were undergoing pulmonary function tests (PFT) or had right heart catheterizations (RHC). Retrospective analysis of the respiratory component of the venous waveform from 8 patients with pulmonary disease (COPD, pulmonary fibrosis, or emphysema: "lung dx") and in 10 controls provided a RIVA-RI that was significantly ($p < 0.05$,) elevated in patients with lung disease, as shown in Figure 7.

[0068] Figure 7 shows a boxplot of difference in RIVA-RI between control and patients with lung disease (A) and RIVA-RI for Idiopathic Pulmonary Fibrosis (B). Venous waveforms were obtained with the NIVA device in patients undergoing right heart catheterization. Retrospective analysis of the respiratory component of the venous waveform from 8 patients with pulmonary disease (COPD, pulmonary fibrosis, or emphysema: "lung dx") and in 10 controls provided a RIVA-RI that was significantly ($p < 0.05$) elevated in patients with lung disease (A). When investigated in IPF, the RIVA-RI was (N=5, median=0.18, IQR 0.14-0.54) compared to pulmonary healthy controls (N=33, median=0.06,

IQR 0.03-0.13). Abbreviations are defined as follows: RIVA-RI= Respiratory non-Invasive Venous waveform Analysis-respiratory index; IPF: idiopathic pulmonary fibrosis. (*)= statistically significant <0.05. There was an elevated RIVA-RI in subjects with the clinical diagnosis of lung disease and in patients with the clinical diagnosis of IPF.

[0069] RIVA-RI was investigated in patients having the clinical diagnosis of Idiopathic Pulmonary Fibrosis (N=5, IPF) and a comparison was conducted to determine the significance between IPF and health controls. Healthy control patients displayed significantly lower RIVA-RI values compared to patients with idiopathic pulmonary fibrosis (IPF; $p < 0.05$). There were no significant correlations between RIVA-RI and any specific value associated with the pulmonary function test (e.g., FEV1, FVC, DLCO), suggesting that RIVA-RI provides a value unique from those obtained with PFT's. Thus, elevated RIVA-RI was associated with chronic pulmonary disease and restrictive diseases (IPF) in particular.

[0070] Finally, RIVA-RI was obtained in four healthy adult patients concurrently with VO_2 max. VO_2 max (mL/kg/min) refers to the intensity of aerobic (oxidative phosphorylation) process and denotes the maximum capacity of transport and utilization of oxygen during exercise at increasing intensities. It is the highest rate of oxygen consumption attainable for a particular individual. At a person's VO_2 max, any additional adenosine triphosphate (ATP) demands must come from other, non-O_2 dependent, metabolic pathways, such as the anaerobic (glycolysis) pathway and the breakdown of pyruvate. VO_2 max, in essence, mimics maximal pulmonary function. Similarly, as a patient's respiratory condition worsens secondary to a pneumonia or COVID-19+ their ability to transport and utilize oxygen worsens requiring oxygen support therapy and more reliance on compensatory metabolic pathways for ATP. When each adult (N=4, Ages= 38 years, 34 years, 22 years, and 21 years) reached their VO_2 max, RIVA-RI increased from a median baseline of 0.03 to a value of 0.78 suggesting that RIVA-RI increases relative to increasing oxygen demand.

[0071] Taken together, these data suggest that RIVA-RI measures the ability to transport and use oxygen at rest and during physical activity (or exertion, work, exercise)." Hence, RIVA-RI may be used to determine and follow trends, in the extent of functional limitation due to pulmonary disease, to assist with diagnosis and management of patients with acute and chronic COVID-19 disease.

[0072] Acquisition, processing, and analysis of the venous waveform using a piezoelectric sensor on the volar aspect of the wrist, uses a unique physiologic signal, the venous waveforms (not simply venous pressure measurements) for monitoring. Deconvolution of a series of waveforms ("window of data over time"), with an algorithm

(fast Fourier transformation), demonstrates the presence of a respiratory signal derived from waves created by retrograde transmission of the negative pressure exerted on the venous system by inspiratory pressures. Weighted contributions of the amplitudes of the frequencies of the pulse rate (f_0) and the respiratory signal (f_{R0}) were used to create a respiratory index ("RIVA-RI"). Preliminary data generated using RIVA-RI suggest that the characteristics of the respiratory signal in the peripheral venous waveform could be used to provide the first point of care, non-invasive device for physiologic monitoring and risk stratification of respiratory disease, including patients with COVID-19.

[0073] Current clinical decision making used to determine the need for hospitalization and/or level of respiratory support in COVID-19 patients is based on respiratory rate (RR, a vital sign), SpO_2 (peripheral capillary oxygen saturation, obtained by pulse oximetry), and clinical judgement. While RIVA-RI had predictive value for predicting the need for supplemental oxygen therapy, both RR and SpO_2 failed to detect need for oxygen therapy (see Figure 6) in COVID-19 patients. The introduction of pulse oximetry was a major advancement in medical monitoring, however there remain problems in SpO_2 demonstrating a lack of specificity in monitoring for acute disease. Respiratory rate has been found to be a very important vital sign for predicting clinical outcomes; however, time and time again its limitations of usage and inaccurate measurements are described. Thus, RIVA-RI value would be the first approach to provide quantitative risk stratification of respiratory physiology, clinically meaningful information to monitor acute respiratory failure, and help triage the need for oxygen therapy in patients with respiratory distress.

[0074] In reviewing venous waveforms in patients with chronic lung disease, elevated RIVA-RI is associated with restrictive chronic pulmonary disease (IPF, see Figure 7). COVID-19 and/or prolonged ventilator use associated with COVID-19 can lead to chronic pulmonary fibrosis and chronic impairment of pulmonary function (one aspect of "long COVID"), suggesting that RIVA-RI may be useful in long term follow up of COVID-19 patients. These preliminary data suggest that RIVA-RI could be used across the spectrum of severe respiratory diseases such as COVID-19.

[0075] With careful clinical analyses, it is likely that RIVA-RI would have additional future uses in monitoring other acute and chronic respiratory diseases such pulmonary fibrosis at home, in the clinic, and in hospital settings. RIVA-RI will likely have further potential to monitor respiratory status in hospitalized patients especially in determining the level of oxygen support needed (oxygen, CPAP, ventilator) and assist in determining how to appropriately decrease that level of oxygen support as respiratory status improves. The ability

to use RIVA-RI in home settings, and the additional monitoring potential that a wristband device with a photodiode and piezoelectric sensor could provide (RR, SpO_2, heart rate, and volume status), suggest that RIVA-RI could be a primary physiologic monitor for telehealth applications in patients with COVID-19, and a variety of other respiratory diseases in the future. The ease of use (disposable wrist patch or reusable wristband), point of care availability, non-invasiveness, and accuracy, position RIVA-RI as a unique and innovative respiratory monitor.

[0076] Figure 8 shows relationships between RIVA-RI to PaO_2 and SpO_2 over time of oleic acid infusion in a porcine model. As acute respiratory distress is induced through direct infusion of oleic acid into the pulmonary artery, RIVA-RI increases as PaO_2 (A) and SpO_2 (B) decreases. When RIVA-RI is visualized in the color spectrum over the entire course of oleic acid infusion, an increase in RIVA-RI value can be seen after 40 minutes of infusion and increasing throughout the development of respiratory distress. Abbreviations are defined as follows: RIVA-RI= Respiratory non-Invasive Venous waveform Analysis Respiratory Index, PaO_2= partial pressure of oxygen, SpO_2= oxygen hemoglobin saturation, min= minutes.

[0077] All the above practices have been successfully demonstrated in the data shown in Figure 8. The model has demonstrated increases in RIVA-RI prior to changes in other respiratory monitoring measures (RR and SpO_2) in patients with COVID. Data also showed that RIVA-RI increases occurred before decreases in PaO_2 and well before decreases in SpO_2 in the porcine model. The ability is confirmed of RIVA-RI to predict the need for subsequent therapeutic oxygen support and determine the RIVA-RI response to ARDS/COVID-19 treatment strategies.

CLAIMS

1. A system comprising:

one or more processors;

a user interface;

a sensor; and

a computer readable medium storing instructions that, when executed by the one or more processors, cause the system to perform functions comprising:

generating, via the sensor, a signal representing vibrations originating from a blood vessel of a patient;

generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations;

identifying a first peak of the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient;

performing a comparison of a first intensity of the first peak with a second intensity of the second peak; and

generating, via the user interface, output indicative of the comparison.

2. The system of claim 1, wherein the sensor comprises a piezioelectric sensor, an optical sensor, a pressure sensor, a force resistive sensor, a tonometer, an ultrasound sensor, a capacitive sensor, or a pressure transducer.

3. The system of any of claims 1-2, wherein the sensor is encapsulated within rubber, a polymer, polyurea, and/or silicone.

4. The system of any of claims 1-3, wherein the sensor is configured to be pressed to a skin of the patient to sense the vibrations.

5. The system of claim 4, wherein the sensor is configured to be pressed to the skin of the patient via positive pressure ranging from 10 mmHg to 60 mmHg to sense the vibrations.

6. The system of any of claims 4-5, further comprising a strap configured to hold the sensor against the skin of the patient.

7. The system of any of claims 1-6, wherein the sensor is configured to be pressed to a wrist, an ankle, an ear canal, an eye, or a neck of the patient to sense the vibrations.

8. The system of any of claims 1-7, wherein the blood vessel comprises a peripheral vein.

9. The system of any of claims 1-8, wherein the blood vessel comprises a peripheral artery.

10. The system of any of claims 1-9, wherein the signal indicates displacement of the sensor with respect to time.

11. The system of any of claims 1-10, wherein generating the intensity spectrum comprises performing a Fourier transform upon the signal.

12. The system of any of claims 1-11, wherein generating the intensity spectrum comprises performing a Fast Fourier transform (FFT) upon the signal.

13. The system of any of claims 1-12, wherein identifying the first peak comprises identifying the first peak as being a most intense peak of any peaks within a range of 0.1 Hz to 0.5 Hz.

14. The system of claim 13, wherein identifying the first peak as being the most intense peak within the range of 0.1 Hz to 0.5 Hz comprises determining that the first peak represents a greatest amount of energy of any peaks within the range of 0.1 Hz to 0.5 Hz.

15. The system of any of claims 1-12, the functions further comprising receiving, via the user interface, an input identifying the first peak, wherein identifying the first peak comprises identifying the first peak based on the input.

16. The system of any of claims 1-12, the functions further comprising receiving from an additional sensor an input identifying the first peak, wherein identifying the first peak comprises identifying the first peak based on the input.

17. The system of any of claims 1-16, wherein identifying the second peak comprises identifying the second peak as being a most intense peak of any peaks within a range of 0.5 Hz to 3.5 Hz.

18. The system of claim 17, wherein identifying the second peak as being the most intense peak within a range of 0.5 Hz to 3.5 Hz comprises determining that the second peak represents a greatest amount of energy of any peaks within the range of 0.5 Hz to 3.5 Hz.

19. The system of any of claims 1-18, the functions further comprising receiving, via the user interface, an input identifying the second peak, wherein identifying the second peak comprises identifying the second peak based on the input.

20. The system of any of claims 1-18, further comprising an additional sensor, the functions further comprising receiving from the additional sensor an input identifying the second peak, wherein identifying the second peak comprises identifying the second peak based on the input.

21. The system of any of claims 1-20, wherein performing the comparison comprises calculating a ratio of the first intensity to the second intensity.

22. The system of claim 21, wherein generating the output comprises generating the output such that the output indicates the ratio.

23. The system of any of claims 1-20, wherein performing the comparison comprises calculating a ratio of the second intensity to the first intensity.

24. The system of claim 23, wherein generating the output comprises generating the output such that the output indicates the ratio.

25. The system of any of claims 1-24, the functions further comprising determining, based on the comparison, a diffusing capacity of the patient's lung for carbon monoxide (DLCO), wherein generating the output comprises generating the output such that the output indicates the DLCO.

26. The system of any of claims 1-25, the functions further comprising determining, based on the comparison, a diffusing capacity of the patient's lung for carbon monoxide divided by an alveolar volume (DLCO/VA), wherein generating the output comprises generating the output such that the output indicates the DLCO/VA.

27. The system of any of claims 1-26, the functions further comprising determining, based on the comparison, an inspiratory reserve volume (IRV) for the patient's lung, wherein generating the output comprises generating the output such that the output indicates the IRV.

28. The system of any of claims 1-27, the functions further comprising determining, based on the comparison, an inspiratory capacity (IC) for the patient's lung, wherein generating the output comprises generating the output such that the output indicates the IC.

29. The system of any of claims 1-28, wherein generating the signal comprises generating the signal such that the signal represents the vibrations that are generated via retrograde transmission of a negative pressure exerted on the patient's venous system by inspiratory pressures.

30. The system of any of claims 1-29, the functions further comprising determining, based on the comparison, whether to administer supplemental oxygen to the patient, wherein generating the output comprises generating the output such that the output indicates whether to administer supplemental oxygen to the patient.

31. The system of any of claims 1-30, the functions further comprising determining, based on the comparison, a maximum rate of oxygen consumption (VO_2 max) for the patient, wherein generating the output comprises generating the output such that the output indicates the VO_2 max.

32. The system of any of claims 1-31, the functions further comprising determining, based on the comparison, a work of breathing for the patient, wherein generating the output comprises generating the output such that the output indicates the work of breathing.

33. The system of any of claims 1-32, the functions further comprising determining, based on the comparison, a pleural pressure for the patient's lung, wherein generating the output comprises generating the output such that the output indicates the pleural pressure.

34. A method comprising:

generating, via a sensor, a signal representing vibrations originating from a blood vessel of a patient;

generating an intensity spectrum of the signal that indicates intensities of the vibrations with respect to oscillation frequencies of the vibrations;

identifying a first peak of the intensity spectrum that corresponds to a respiratory frequency of the patient and a second peak of the intensity spectrum that corresponds to a heart rate of the patient;

performing a comparison of a first intensity of the first peak with a second intensity of the second peak; and

generating, via a user interface, output indicative of the comparison.

35. The method of claim 34, further comprising pressing the sensor to a skin of the patient while generating the signal.

36. The method of claim 35, wherein pressing the sensor to the skin comprises pressing the sensor to the skin at 10 mmHg to 60 mmHg.

37. The method of any of claims 34-36, wherein pressing the sensor to the skin comprises pressing the sensor to a wrist, an ankle, an ear canal, an eye, or a neck of the patient.

38. The method of any of claims 34-37, wherein the blood vessel comprises a peripheral vein.

39. The method of any of claims 34-37, wherein the blood vessel comprises a peripheral artery.

40. The method of any of claims 34-39, wherein the signal indicates displacement of the sensor with respect to time.

41. The method of any of claims 34-340, wherein generating the intensity spectrum comprises performing a Fourier transform upon the signal.

42. The method of any of claims 34-41, wherein generating the intensity spectrum comprises performing a Fast Fourier transform (FFT) upon the signal.

43. The method of any of claims 34-42, wherein identifying the first peak comprises identifying the first peak as being a most intense peak of any peaks within a range of 0.1 Hz to 0.5 Hz.

44. The method of claim 43, wherein identifying the first peak as being the most intense peak within the range of 0.1 Hz to 0.5 Hz comprises determining that the first peak represents a greatest amount of energy of any peaks within the range of 0.1 Hz to 0.5 Hz.

45. The method of any of claims 34-44, further comprising receiving, via the user interface, an input identifying the first peak, wherein identifying the first peak comprises identifying the first peak based on the input.

46. The method of any of claims 34-45, further comprising receiving from an additional sensor an input identifying the first peak, wherein identifying the first peak comprises identifying the first peak based on the input.

47. The method of any of claims 34-46, wherein identifying the second peak comprises identifying the second peak as being a most intense peak of any peaks within a range of 0.5 Hz to 3.5 Hz.

48. The method of claim 47, wherein identifying the second peak as being the most intense peak within a range of 0.5 Hz to 3.5 Hz comprises determining that the second peak represents a greatest amount of energy of any peaks within the range of 0.5 Hz to 3.5 Hz.

49. The method of any of claims 34-48, further comprising receiving, via the user interface, an input identifying the second peak, wherein identifying the second peak comprises identifying the second peak based on the input.

50. The method of any of claims 34-48, further comprising receiving from an additional sensor an input identifying the second peak, wherein identifying the second peak comprises identifying the second peak based on the input.

51. The method of any of claims 34-50, wherein performing the comparison comprises calculating a ratio of the first intensity to the second intensity.

52. The method of claim 51, wherein generating the output comprises generating the output such that the output indicates the ratio.

53. The method of any of claims 34-52, wherein performing the comparison comprises calculating a ratio of the second intensity to the first intensity.

54. The method of claim 53, wherein generating the output comprises generating the output such that the output indicates the ratio.

55. The method of any of claims 34-54, further comprising determining, based on the comparison, a diffusing capacity of the patient's lung for carbon monoxide (DLCO).

56. The method of claim 55, wherein generating the output comprises generating the output such that the output indicates the DLCO.

57. The method of any of claims 34-56, further comprising determining based on the comparison, a diffusing capacity of the patient's lung for carbon monoxide divided by an alveolar volume (DLCO/VA).

58. The method of claim 57, wherein generating the output comprises generating the output such that the output indicates the DLCO/VA.

59. The method of any of claims 34-58, further comprising determining, based on the comparison, an inspiratory reserve volume (IRV) for the patient's lung.

60. The method of claim 59, wherein generating the output comprises generating the output such that the output indicates the IRV.

61. The method of any of claims 34-60, further comprising determining, based on the comparison, an inspiratory capacity (IC) for the patient's lung.

62. The method of claim 61, wherein generating the output comprises generating the output such that the output indicates the IC.

63. The method of any of claims 34-62, further comprising determining, based on the comparison, a maximum rate of oxygen consumption (VO_2 max).

64. The method of claim 63, wherein generating the output comprises generating the output such that the output indicates the VO_2 max.

65. The method of any of claims 34-64, further comprising determining, based on the comparison, a work of breathing for the patient.

66. The method of claim 65, wherein generating the output comprises generating the output such that the output indicates the work of breathing.

67. The method of claims of 34-66, further comprising determining, based on the comparison, a pleural pressure for the patient's lung.

68. The method of claim 67, wherein generating the output comprises generating the output such that the output indicates the pleural pressure.

69. The method of any of claims 34-68, further comprising commencing, adjusting, or ceasing a treatment for the patient based on the comparison.

70. The method of claim 69, wherein commencing, adjusting, or ceasing the treatment comprises adjusting a dosage, frequency, or duration of an oxygen treatment for the patient.

71. The method of any of claims 56-70, wherein commencing, adjusting, or ceasing the treatment comprises commencing, adjusting, or ceasing a continuous positive airway pressure (CPAP) treatment for the patient.

72. The method of any of claims 34-71, wherein the patient is experiencing a pulmonary disease.

73. The method of claim 72, wherein the pulmonary disease is chronic obstructive pulmonary disease (COPD), restrictive chronic pulmonary disease, COVID-19, sleep apnea, bronchiectasis, asthma, pulmonary edema, congestion, pneumothorax, pneumonia, reaction to allergens, medicinal overdoses/side-effects, airway obstruction, pulmonary edema, cerebral vascular accidents, spinal cord injuries, opioid overdose/misuse, inhalational injuries, Guillain-barre syndrome, myasthenia gravis, amyotrophic lateral sclerosis (ALS), cystic fibrosis, sepsis, respiratory distress, hypoxia, or pulmonary fibrosis.

74. The method of any of claims 34-73, wherein generating the signal comprises generating the signal such that the signal represents the vibrations that are generated via retrograde transmission of a negative pressure exerted on the patient's venous system by inspiratory pressures.

75. The method of any of claims 34-74, the functions further comprising determining, based on the comparison, whether to administer supplemental oxygen to the patient, wherein generating the output comprises generating the output such that the output indicates whether to administer supplemental oxygen to the patient.

76. The method of any of claims 34-75, wherein the method is performed at least in part by the system of any of claims 1-33.

77. A non-transitory computer readable medium storing instructions that, when executed by the system of any of claims 1-33, cause the system to perform the method of any of claims 34-75.

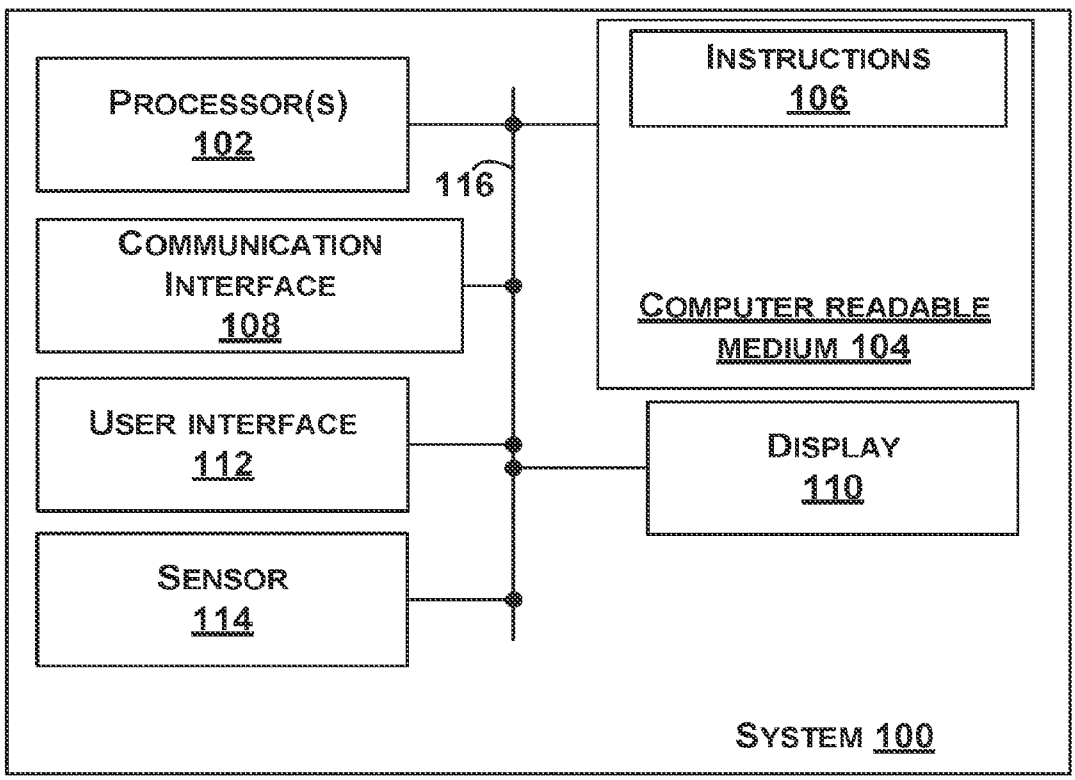
PROCESSOR(S)
102
INSTRUCTIONS
106
116
COMMUNICATION
INTERFACE
108
COMPUTER READABLE
MEDIUM 104
USER INTERFACE
112
DISPLAY
110
SENSOR
114
SYSTEM 100

FIG. 1

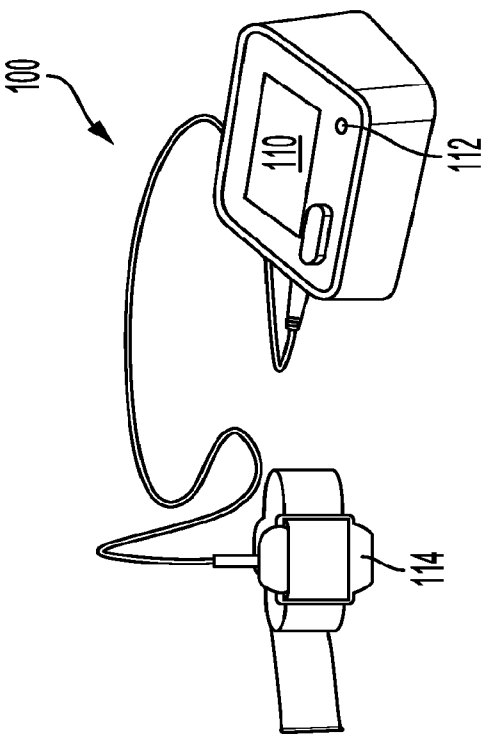

FIG. 2

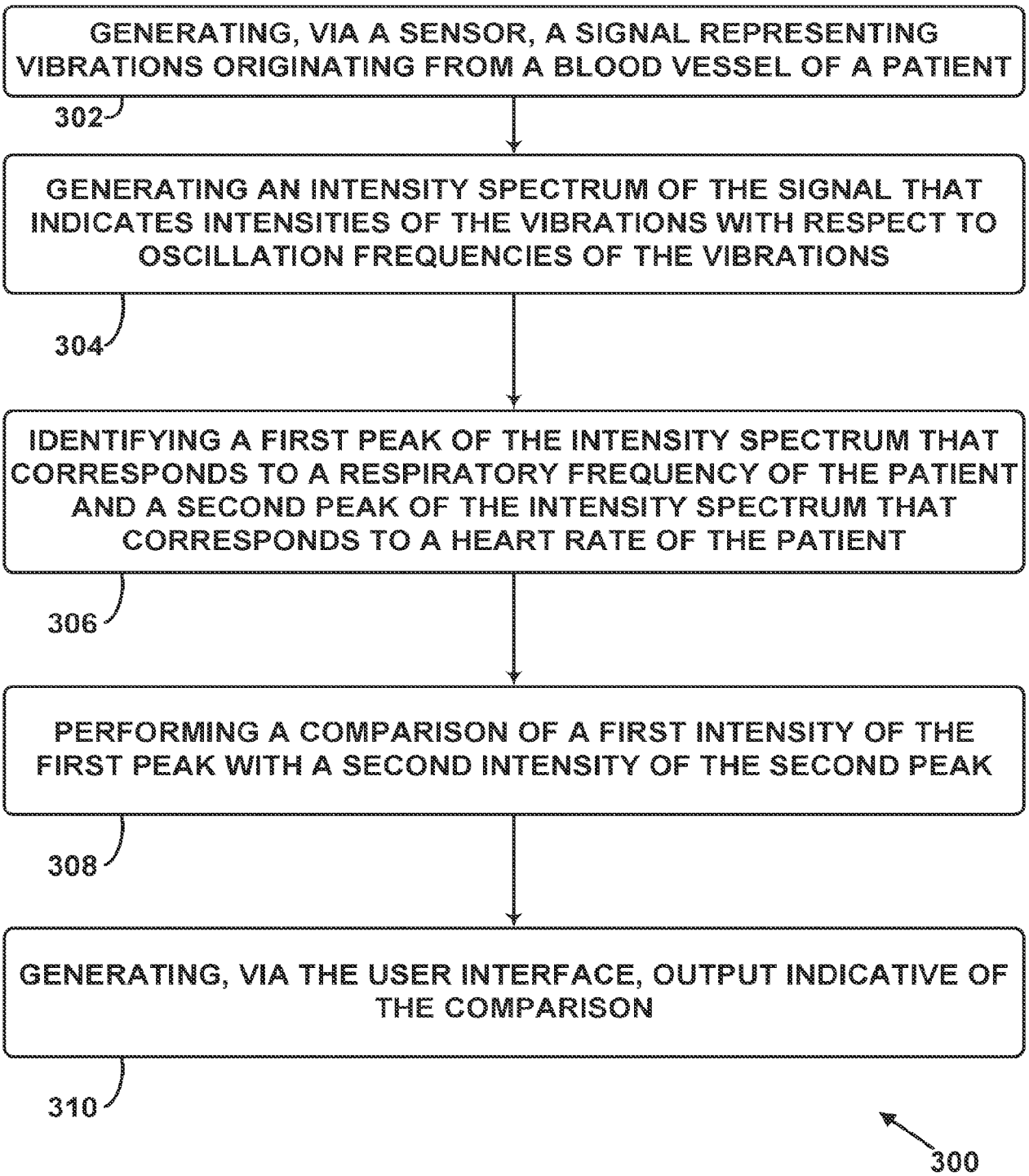
GENERATING, VIA A SENSOR, A SIGNAL REPRESENTING VIBRATIONS ORIGINATING FROM A BLOOD VESSEL OF A PATIENT
302
GENERATING AN INTENSITY SPECTRUM OF THE SIGNAL THAT INDICATES INTENSITIES OF THE VIBRATIONS WITH RESPECT TO OSCILLATION FREQUENCIES OF THE VIBRATIONS
304
IDENTIFYING A FIRST PEAK OF THE INTENSITY SPECTRUM THAT CORRESPONDS TO A RESPIRATORY FREQUENCY OF THE PATIENT AND A SECOND PEAK OF THE INTENSITY SPECTRUM THAT CORRESPONDS TO A HEART RATE OF THE PATIENT
306
PERFORMING A COMPARISON OF A FIRST INTENSITY OF THE FIRST PEAK WITH A SECOND INTENSITY OF THE SECOND PEAK
308
GENERATING, VIA THE USER INTERFACE, OUTPUT INDICATIVE OF THE COMPARISON
310
300

FIG. 3

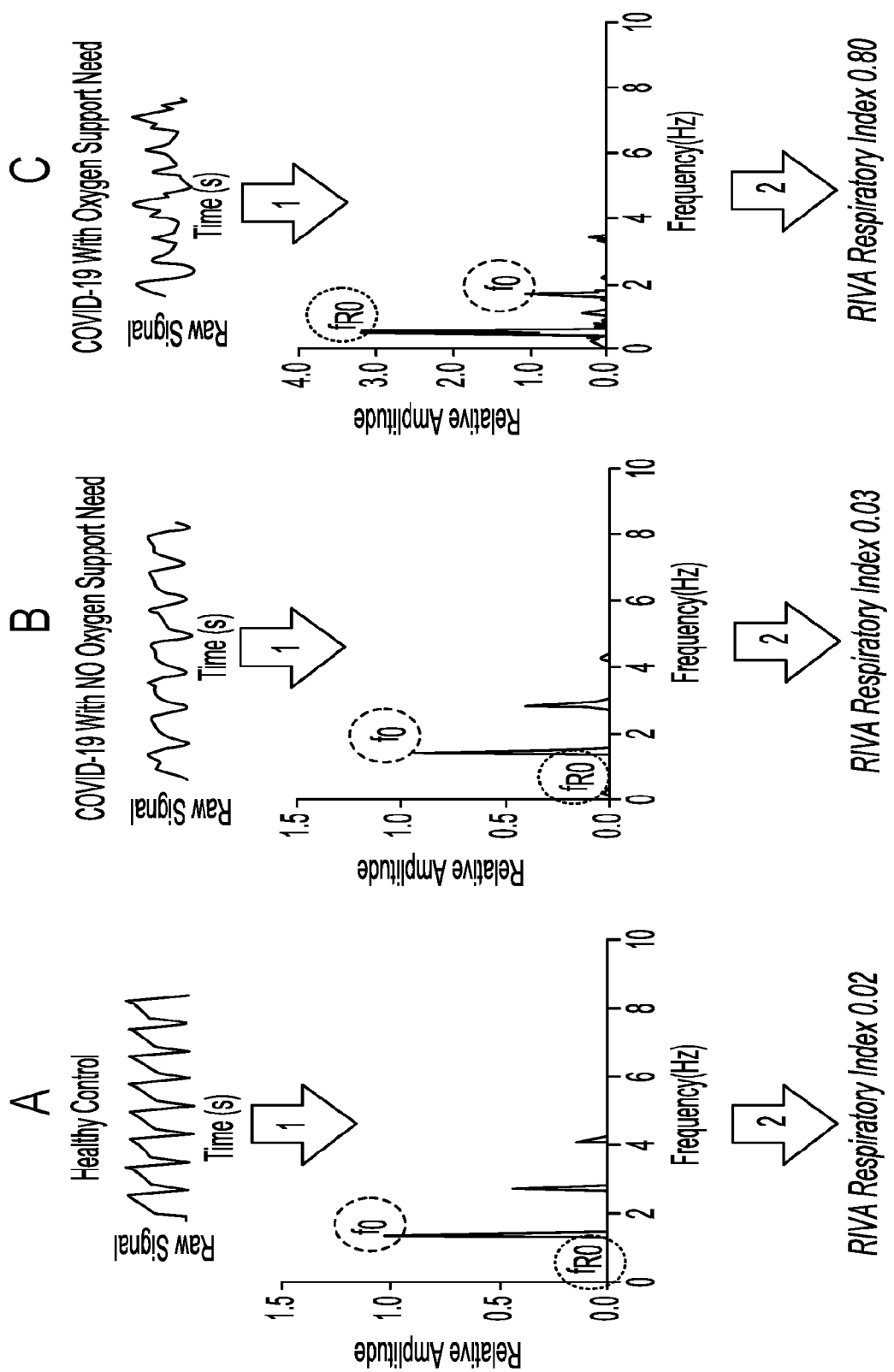
A
Healthy Control
Raw Signal
Time (s)
1
Relative Amplitude
Frequency(Hz)
fo
fRO
2
RIVA Respiratory Index 0.02
B
COVID-19 With NO Oxygen Support Need
Raw Signal
Time (s)
1
Relative Amplitude
Frequency(Hz)
fo
fRO
2
RIVA Respiratory Index 0.03
C
COVID-19 With Oxygen Support Need
Raw Signal
Time (s)
1
Relative Amplitude
Frequency(Hz)
fo
fRO
2
RIVA Respiratory Index 0.80

FIG. 4

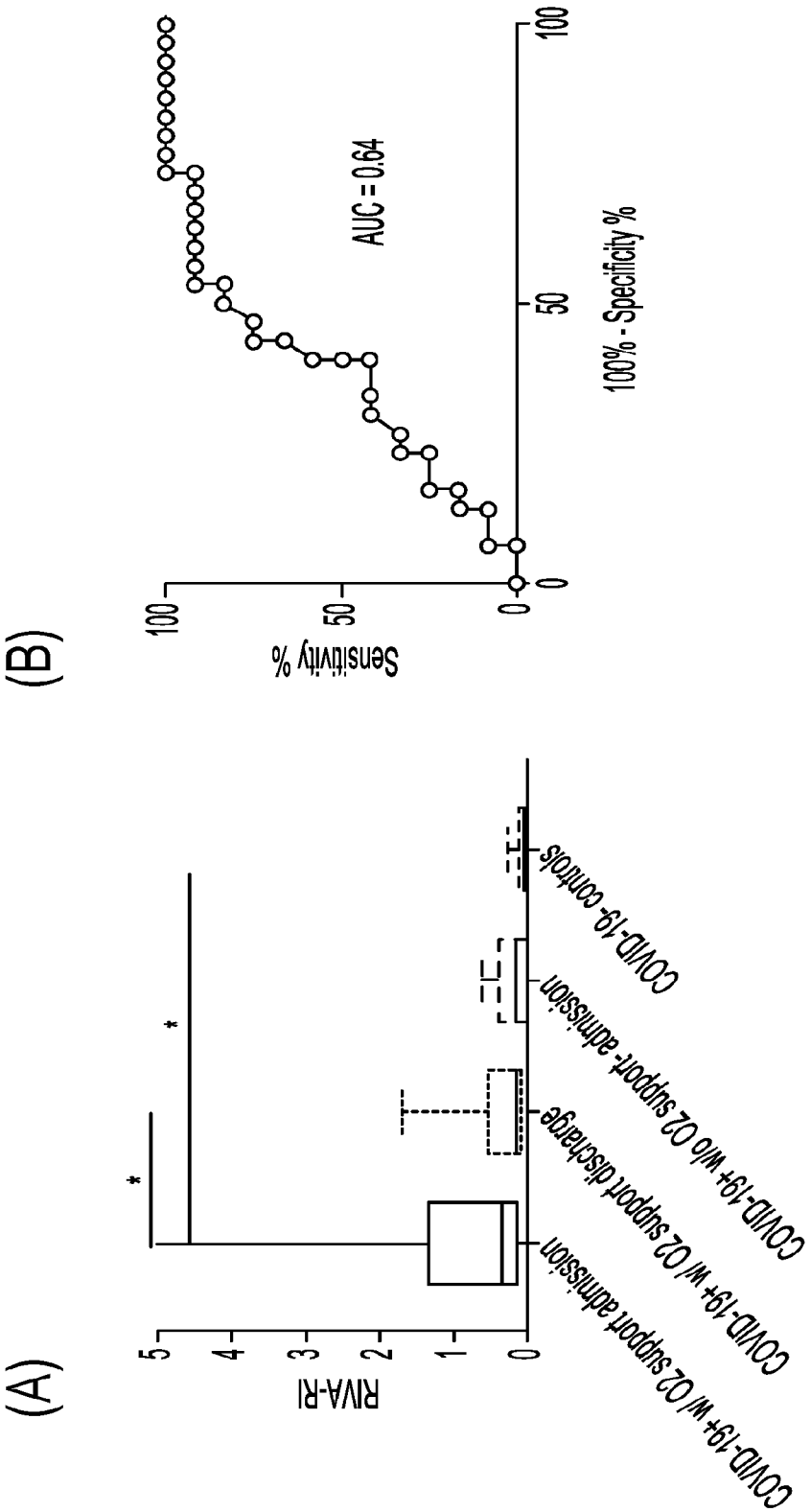
(A)
RIVA-RI
0
1
2
3
4
5
*
*
COVID-19+ W/ O2 support admission
COVID-19+ W/ O2 support discharge
COVID-19+ W/o O2 support- admission
COVID-19- controls
(B)
Sensitivity %
0
50
100
AUC = 0.64
0
50
100
100% - Specificity %

FIG. 5

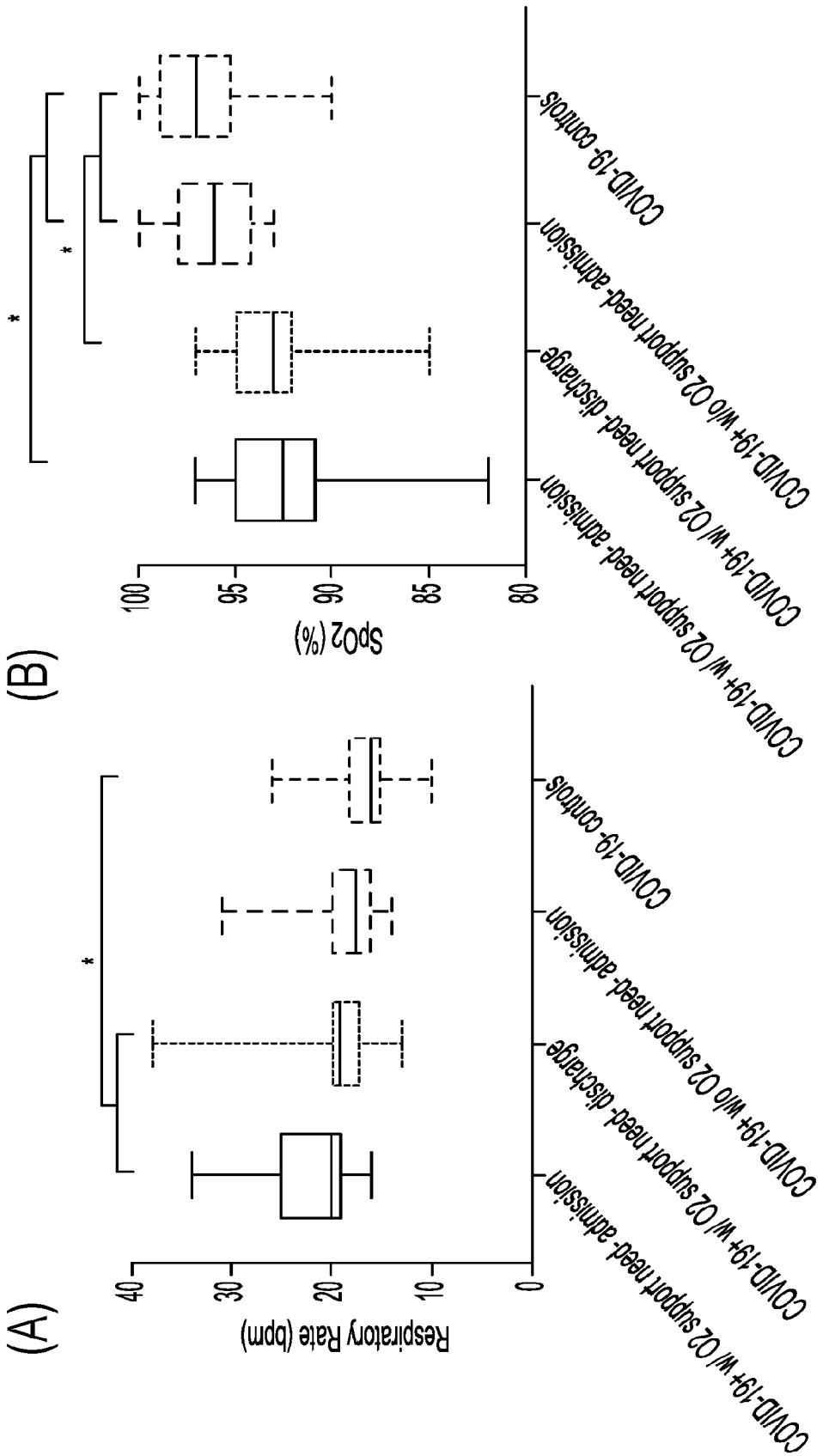
(A)
Respiratory Rate (bpm)
0
10
20
30
40
*
COVID-19+ w/ O2 support need- admission
COVID-19+ w/ O2 support need- discharge
COVID-19+ w/o O2 support need- admission
COVID-19- controls
(B)
SpO2 (%)
80
85
90
95
100
*
*
COVID-19+ w/ O2 support need- admission
COVID-19+ w/ O2 support need- discharge
COVID-19+ w/o O2 support need- admission
COVID-19- controls

FIG. 6

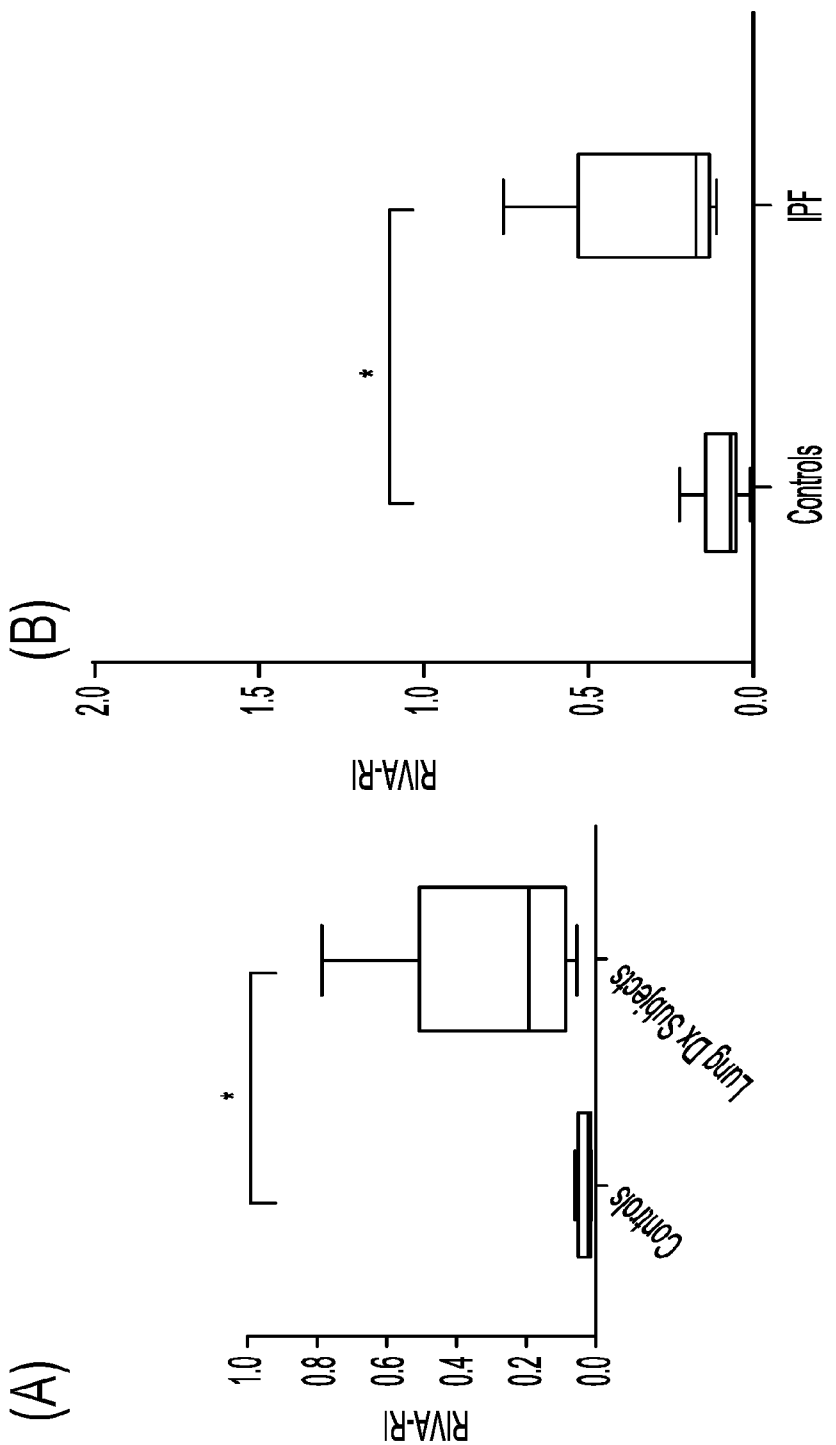
(A)
RIVA-RI
1.0
0.8
0.6
0.4
0.2
0.0
*
Controls
Lung DX Subjects
(B)
RIVA-RI
2.0
1.5
1.0
0.5
0.0
*
Controls
IPF

FIG. 7

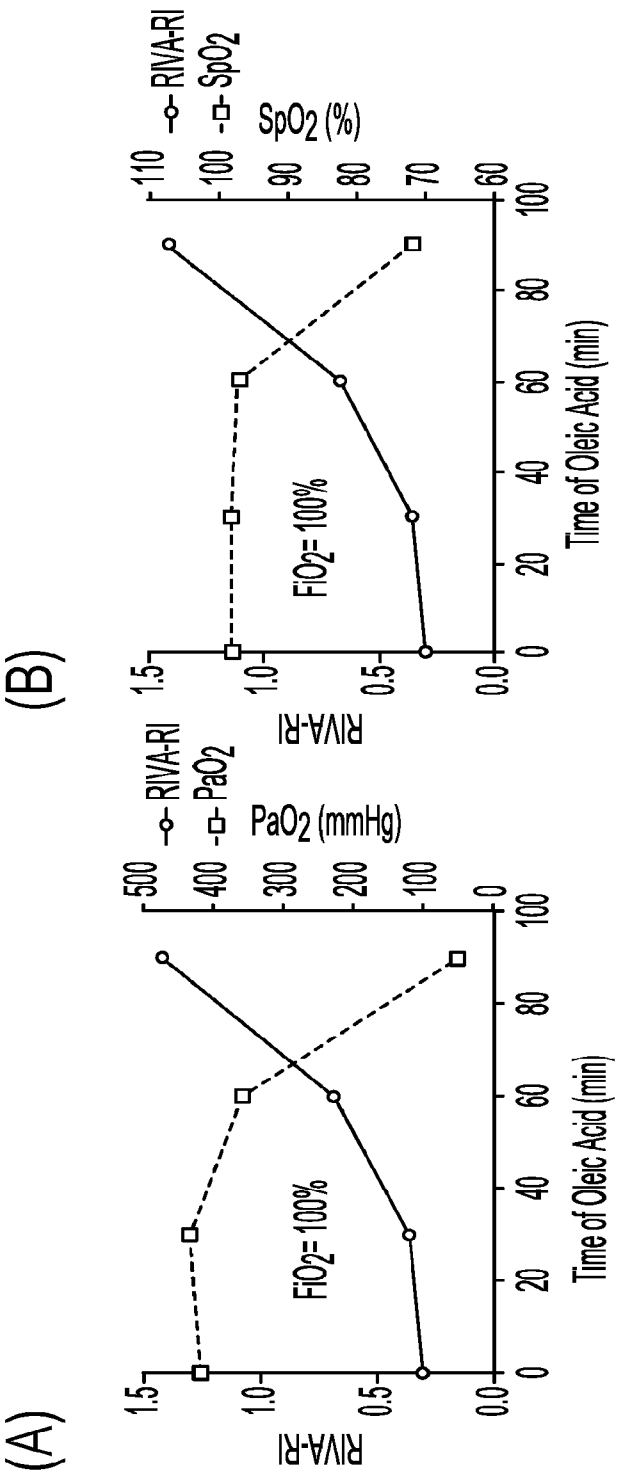
(A)
RIVA-RI
PaO2 (mmHg)
RIVA-RI
PaO2
FiO2= 100%
Time of Oleic Acid (min)
(B)
RIVA-RI
SpO2 (%)
RIVA-RI
SpO2
FiO2= 100%
Time of Oleic Acid (min)

FIG. 8

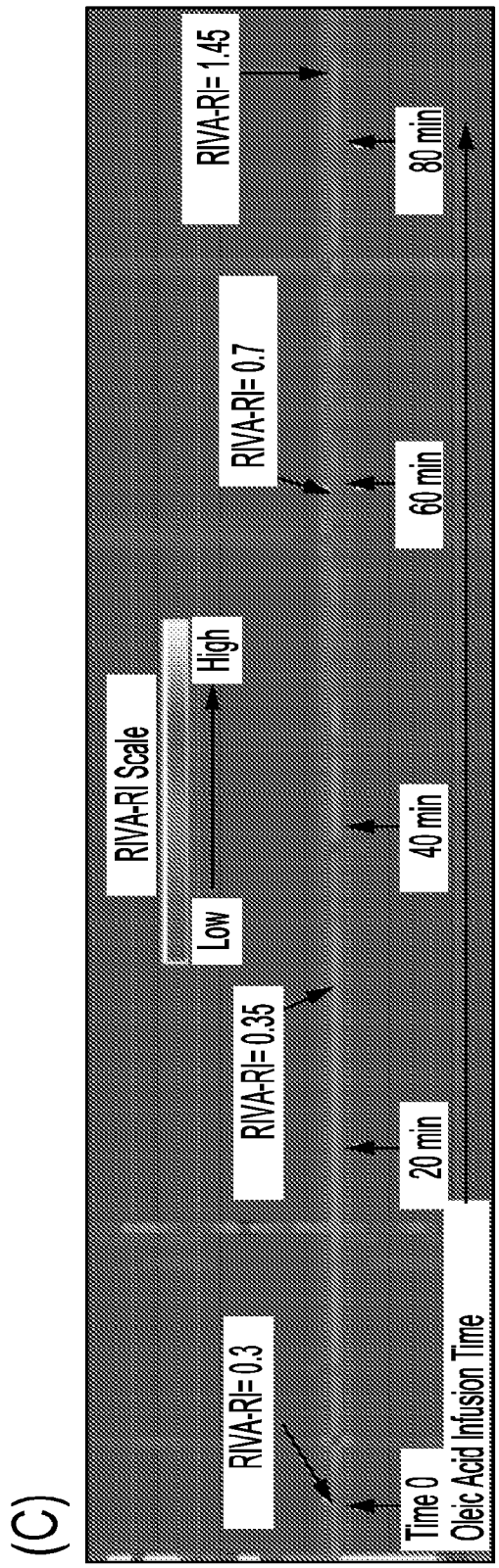

FIG. 8
CONTINUED

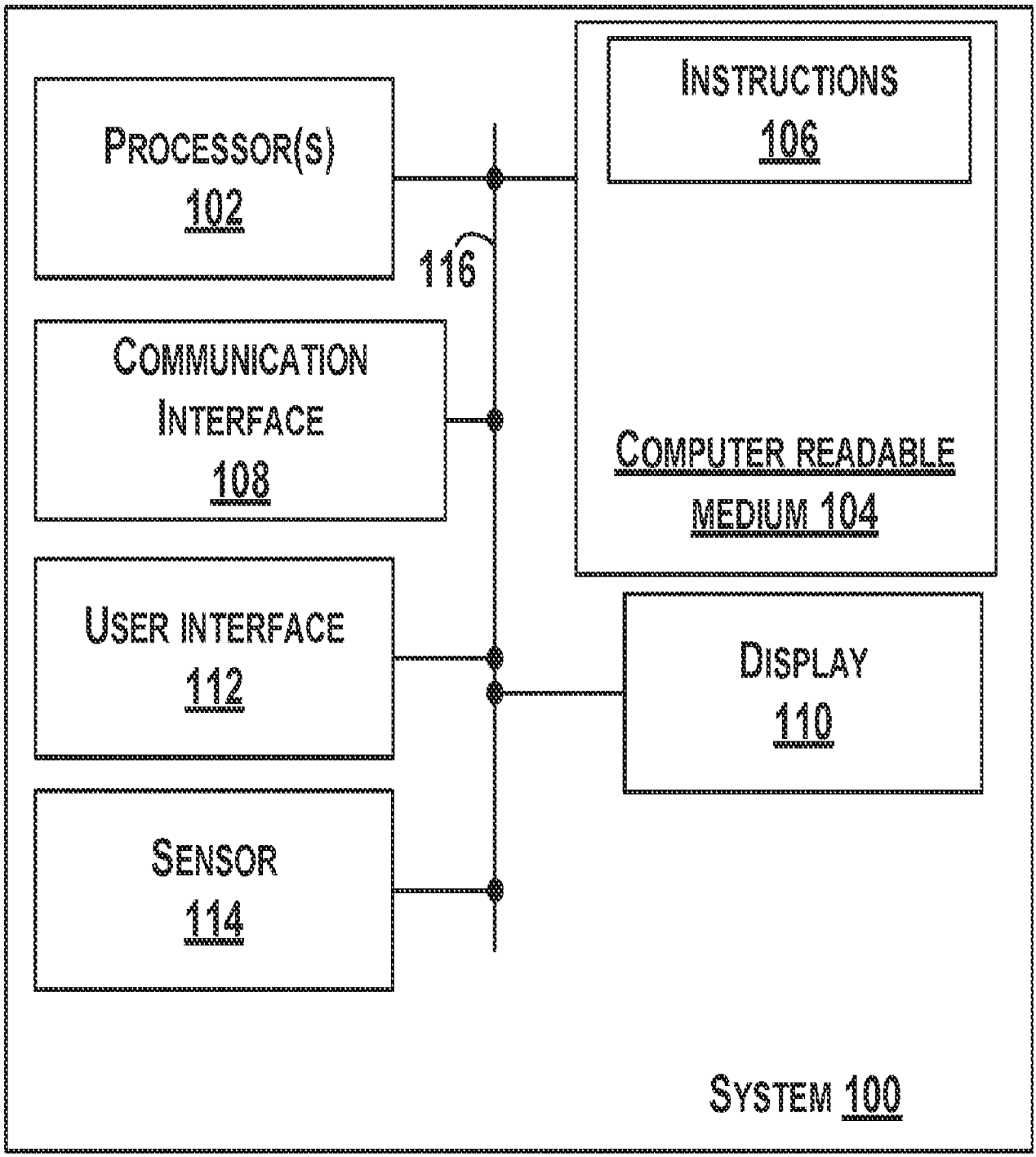
PROCESSOR(S)
102
INSTRUCTIONS
106
116
COMMUNICATION
INTERFACE
108
COMPUTER READABLE
MEDIUM 104
USER INTERFACE
112
DISPLAY
110
SENSOR
114
SYSTEM 100

FIG. 1