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(54) **END-TIDAL CARBON DIOXIDE AND AMPLITUDE SPECTRAL AREA AS NON-INVASIVE MARKERS OF CORONARY PERFUSION PRESSURE**

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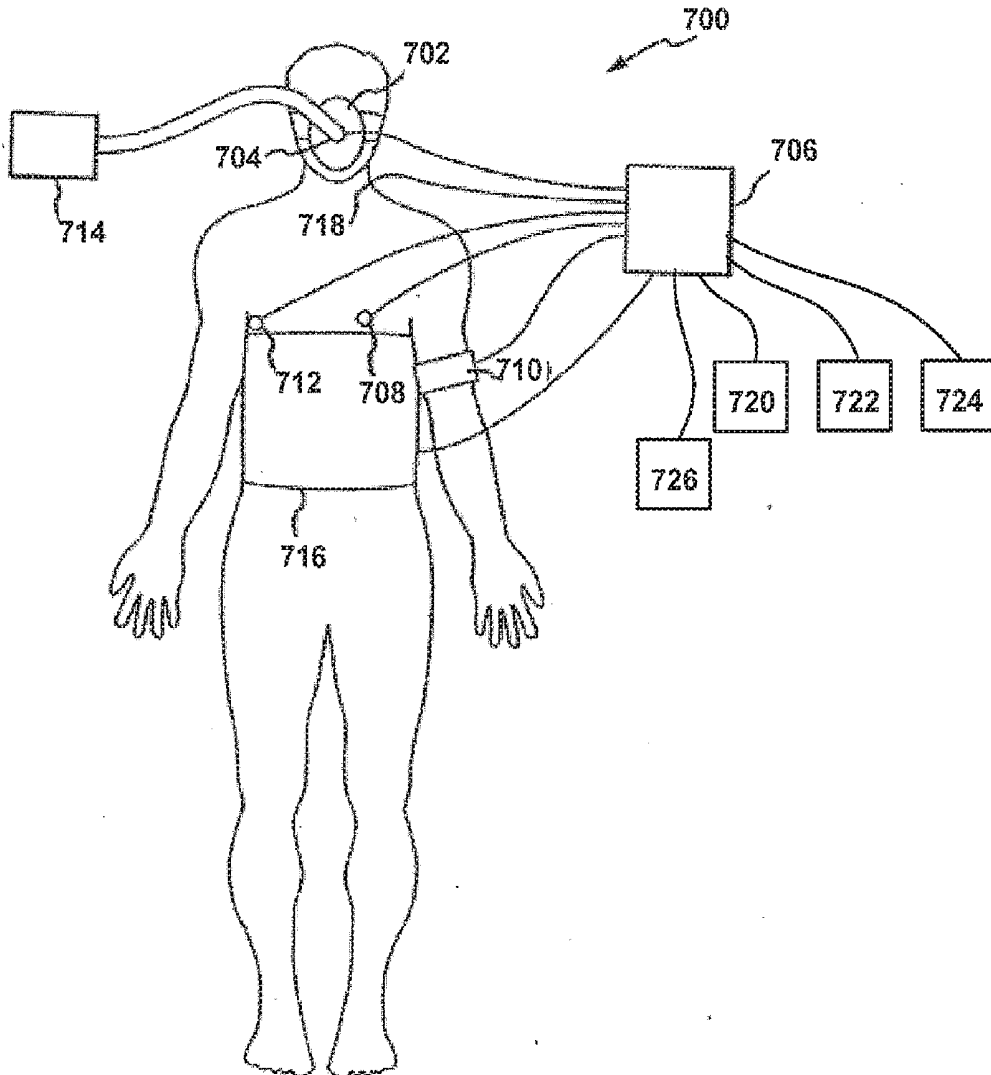
**Related U.S. Application Data**

(63) Continuation of application No. 14/292,578, filed on May 30, 2014, now abandoned.

(60) Provisional application No. 61/829,176, filed on May 30, 2013.

(57) **ABSTRACT**

End-tidal carbon dioxide (ETCO<sub>2</sub>) measurements may be used alone as a guide to determine when to defibrillate an individual. Alternatively, ETCO<sub>2</sub> measurements may be used in combination with amplitude spectral area measurements as a guide to determine when to defibrillate an individual.



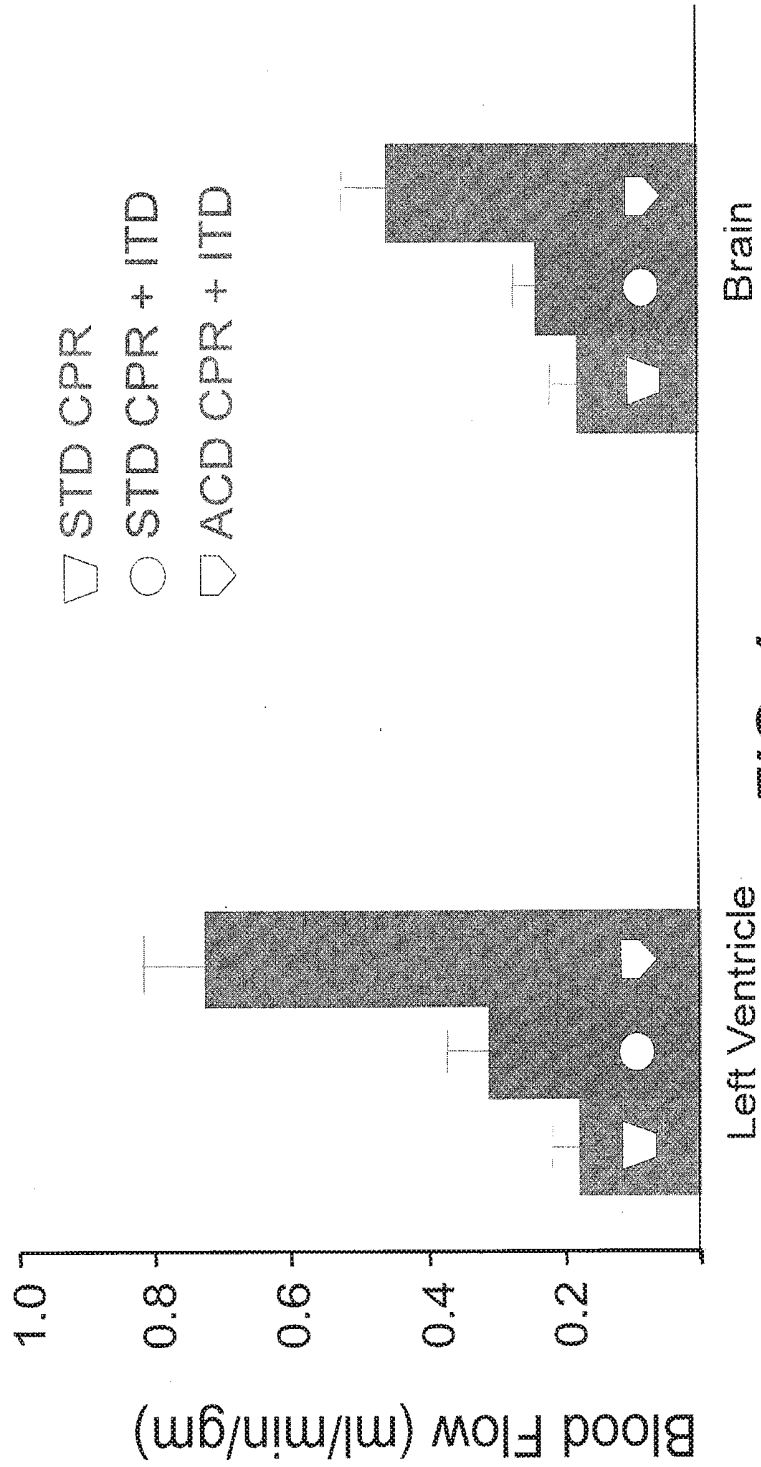
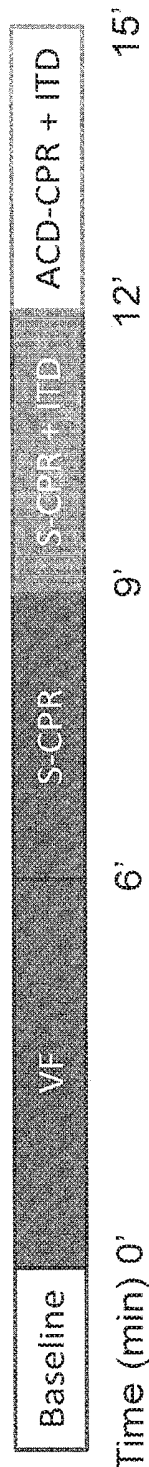
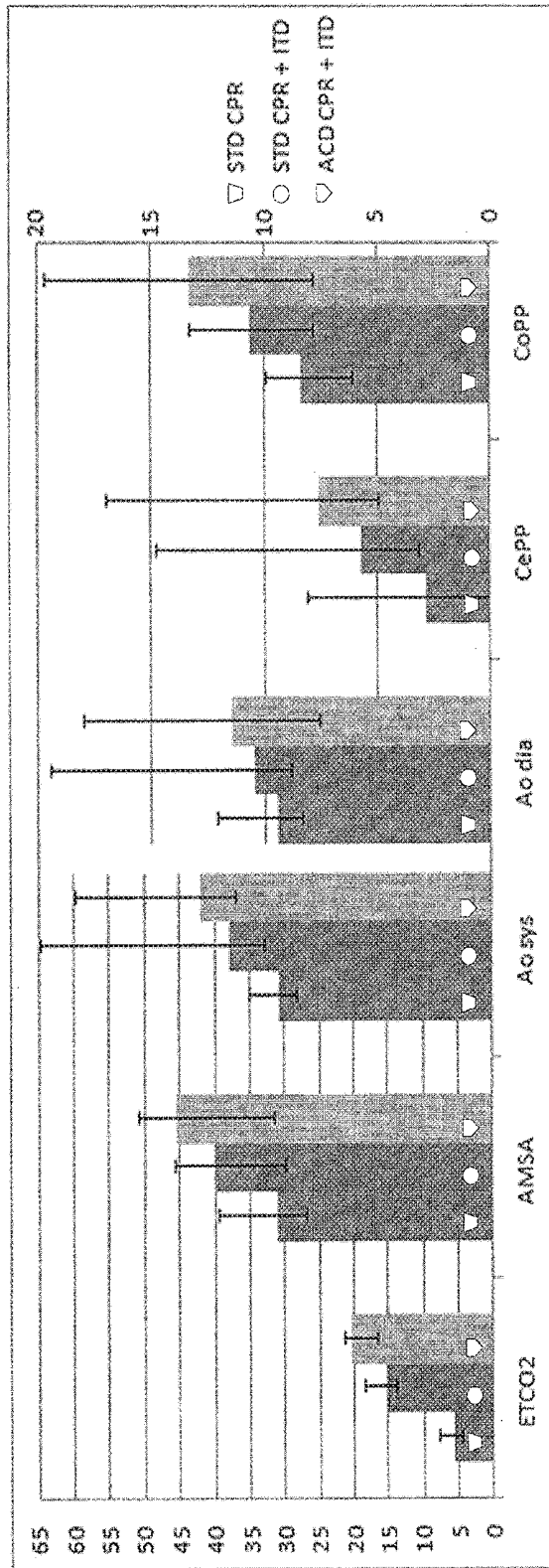


FIG. 1

- Swine model: 12 female farm pigs (32±1Kg)
  - Anesthetic: ketamine followed by isoflurane
  - 6 min untreated VF
  - 3 min sequential CPR epochs
    - standard (S) CPR,
    - S-CPR + an impedance threshold device (ITD),
    - active compression decompression (ACD) + ITD CPR.



**FIG. 2**



Median ± 25; 75 percentile

**FIG. 3**

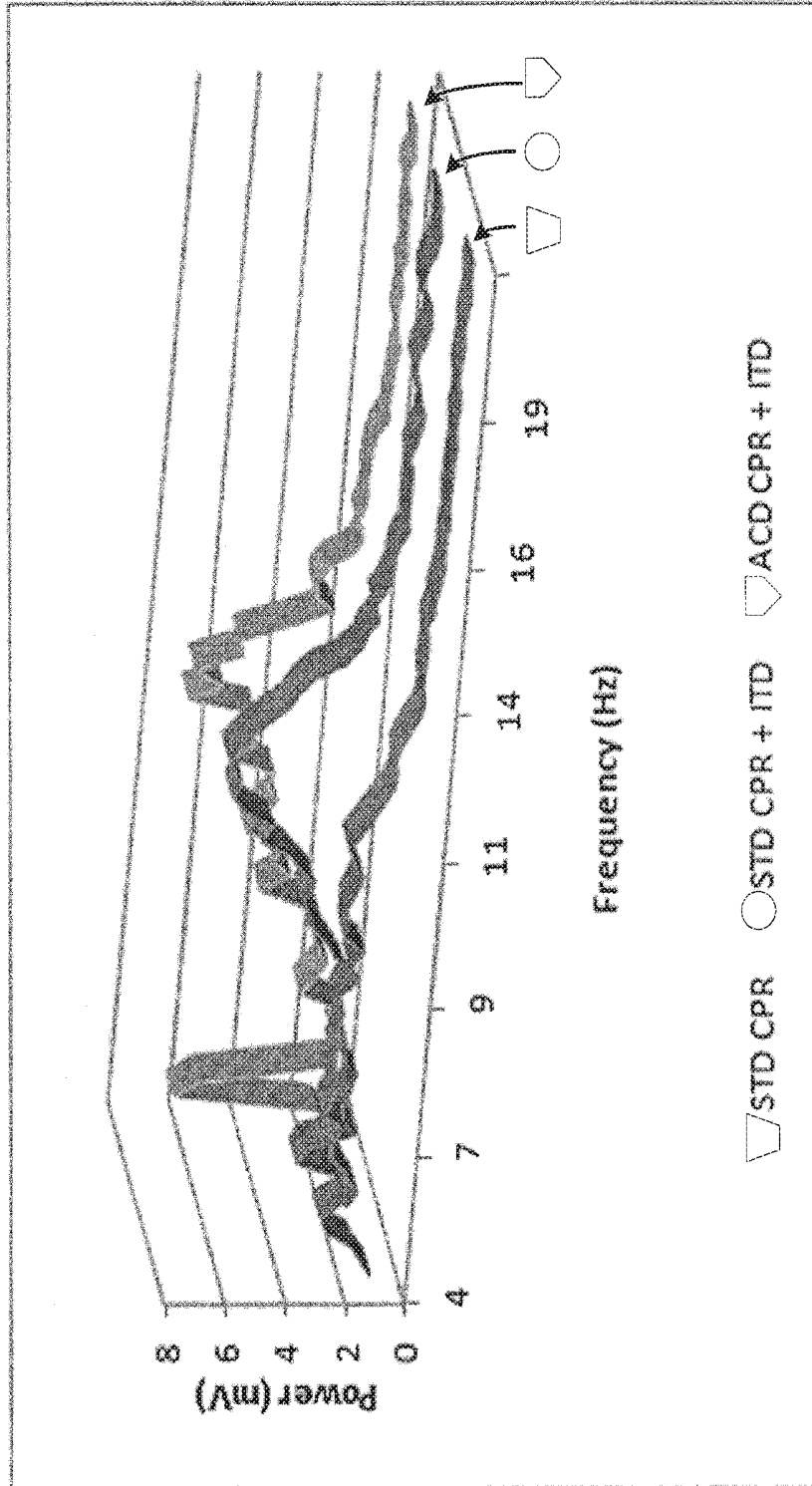


FIG. 4

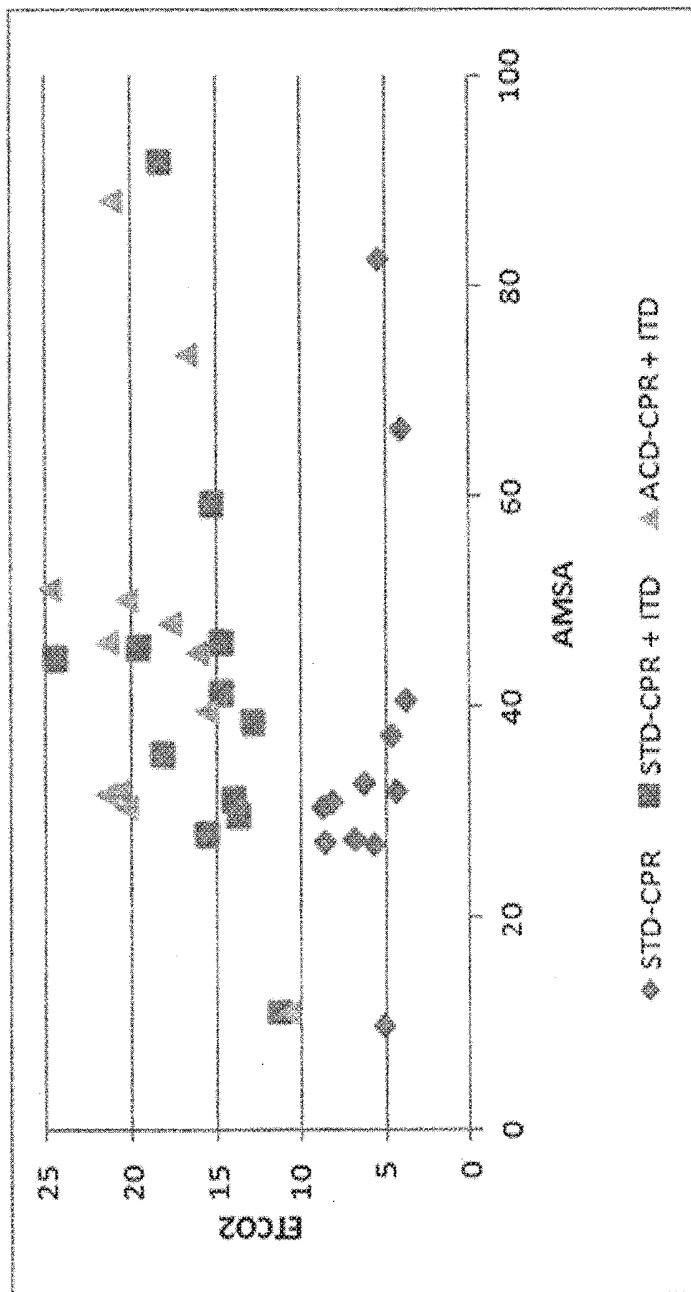


FIG. 5

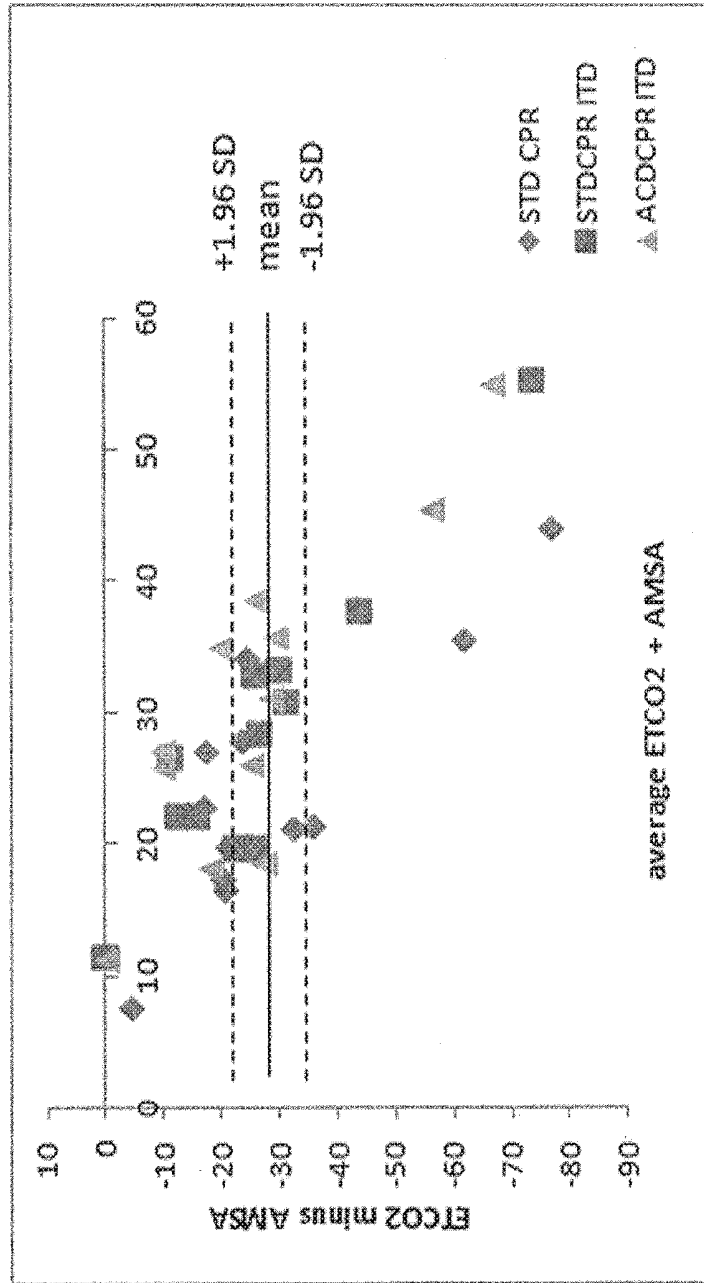


FIG. 6

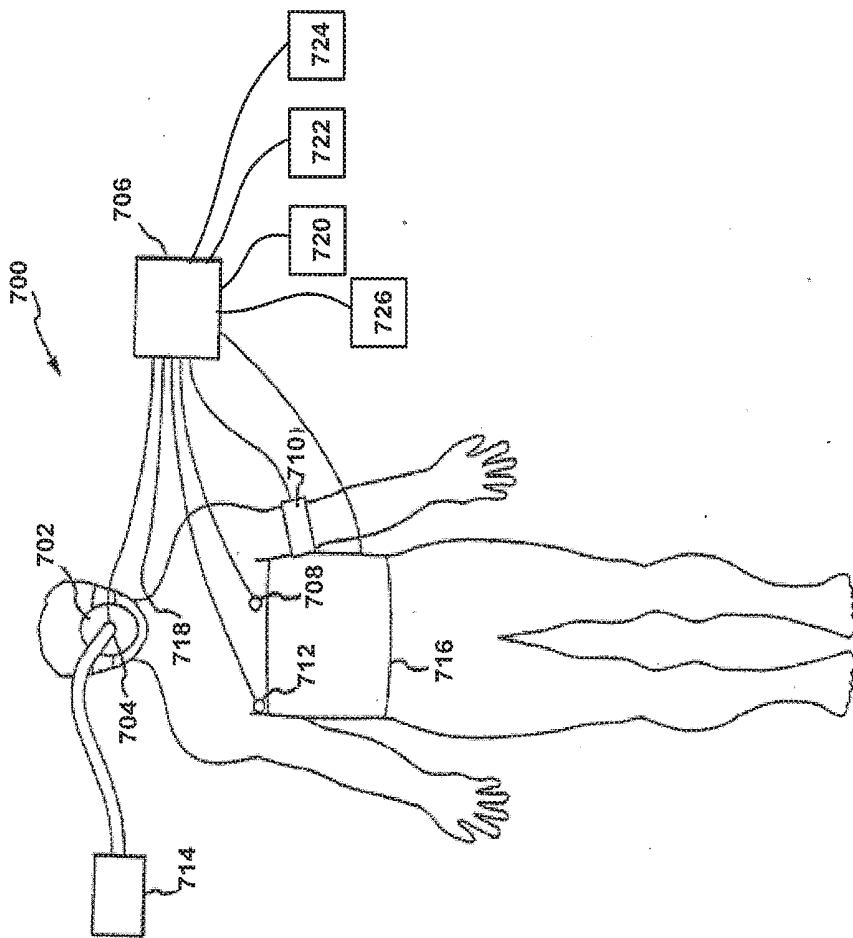


FIG. 7

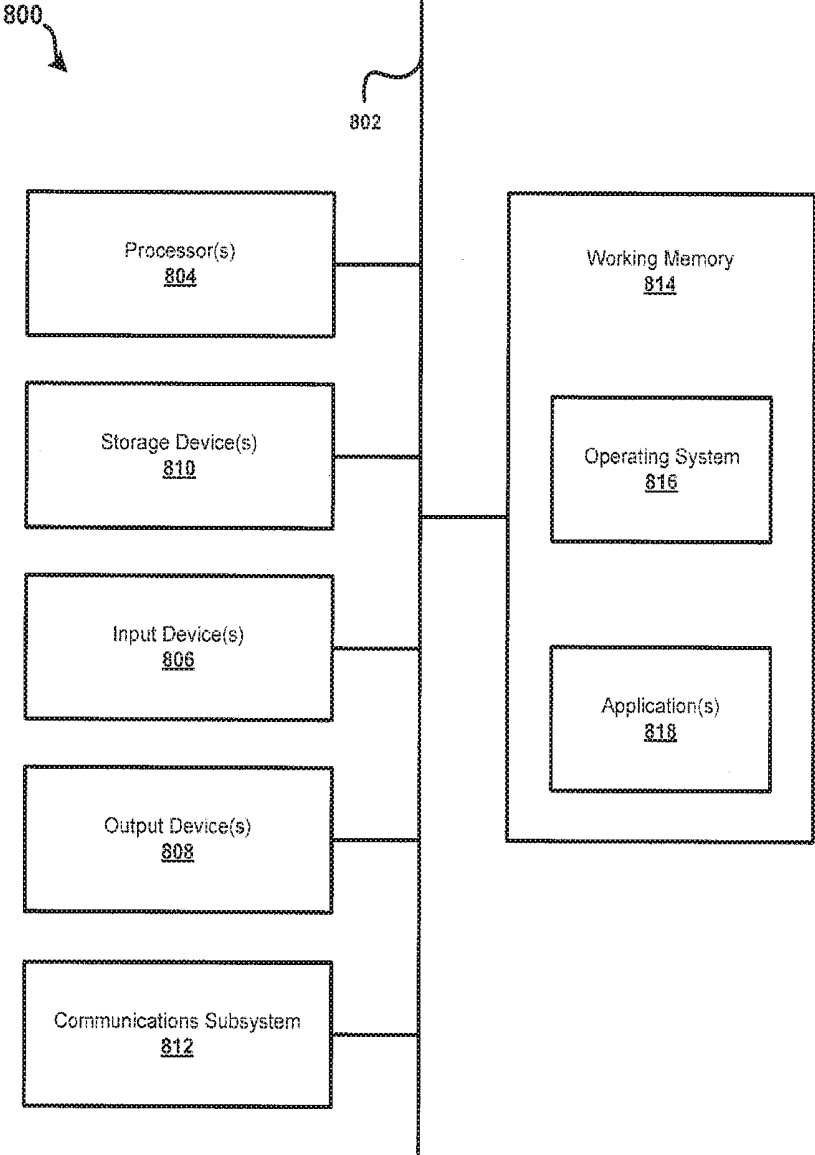


FIG. 8

**END-TIDAL CARBON DIOXIDE AND  
AMPLITUDE SPECTRAL AREA AS  
NON-INVASIVE MARKERS OF CORONARY  
PERFUSION PRESSURE**

CROSS-REFERENCE TO RELATED  
APPLICATIONS

**[0001]** This application is a continuation of co-pending U.S. patent application Ser. No. 14/292,578, filed May 30, 2014, which claims priority to U.S. Provisional Patent Application No. 61/829,176 filed May 30, 2013, entitled END TIDAL CARBON DIOXIDE AND AMPLITUDE SPECTRAL AREA AS NON-INVASIVE MARKERS OF CORONARY PERFUSION PRESSURE AND ARTERIAL PRESSURE, the entire disclosures of which are hereby incorporated by reference, for all purposes, as if fully set forth herein.

SUMMARY

**[0002]** Amplitude Spectrum Area (AMSA) values during ventricular fibrillation (VF) correlate with myocardial energy stores and predict defibrillation success. AMSA calculations however require particular hardware and/or software, and are clinically not used to determine an optimal time to deliver a defibrillation shock. By contrast, end tidal CO<sub>2</sub>(ETCO<sub>2</sub>) values provide a non-invasive assessment of circulation during cardiopulmonary resuscitation (CPR). Accordingly, it is contemplated that ETCO<sub>2</sub> measurements alone or in combination with AMSA values may be utilized as a non-invasive means to determine an optimal time to deliver defibrillation during cardiac arrest and CPR. This is supported by acquired data that demonstrates a positive correlation between AMSA and ETCO<sub>2</sub>, as discussed throughout. In particular, it has been demonstrated that AMSA and ETCO<sub>2</sub> correlate with each other and can be used to correlate with myocardial perfusion. This correlation may be used as a way to provide additional support for more widespread use of ETCO<sub>2</sub> to help guide defibrillation therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

**[0003]** FIG. 1 shows blood flow during multiple different CPR methods (porcine VF model).

**[0004]** FIG. 2 shows details of a model used to demonstrate AMSA and ETCO<sub>2</sub> correlation.

**[0005]** FIG. 3 shows parameter results using three different CPR techniques.

**[0006]** FIG. 4 shows a representative spectrum from a porcine model during each of three methods of CPR.

**[0007]** FIG. 5 demonstrates a correlation between AMSA and ETCO<sub>2</sub>.

**[0008]** FIG. 6 shows results of Bland-Altman analysis indicating the 95% limits of agreement between AMSA and ETCO<sub>2</sub> ranged from -21.4 to -33.5.

**[0009]** FIG. 7 shows an example treatment system in accordance with the present disclosure.

**[0010]** FIG. 8 shows an example computing system or device.

DETAILED DESCRIPTION

**[0011]** Using multiple CPR methods to generate several different levels of coronary perfusion and cerebral perfusion, a correlation between ETCO<sub>2</sub> and AMSA values is identi-

fied. The data establishes a firm correlation between ETCO<sub>2</sub> and AMSA, and demonstrates that ETCO<sub>2</sub> may be useful as an independent indicator as to when to deliver a defibrillation shock. In particular, in one example embodiment, ETCO<sub>2</sub> measurements may be used alone as a guide to determine when to defibrillate an individual. In another example embodiment, ETCO<sub>2</sub> measurements may be used in combination with AMSA values as a guide to determine when to defibrillate an individual. Although not so limited, an appreciation of the various aspects of the disclosure may be acquired from the following description in connection with the drawings.

**[0012]** The International Consensus on Cardiopulmonary Resuscitation 2010 recommends delivering a defibrillation shock every two minutes during treatment of cardiac arrest. The magnitude of the electrical energy of the delivered shock, however, has been demonstrated to be related to the severity of post-resuscitation global myocardial dysfunction. Additionally, interruptions in precordial compressions have been determined to reduce coronary perfusion pressures (CoPP) which may compromise the success of the shocks, especially after prolonged cardiac arrest. To limit the number of unnecessary shocks and interruptions in precordial compressions, VF waveform analysis has been established to predict the success of defibrillation at any given time. Several different analysis methods have been developed and the most efficient of these methodologies is to examine the AMSA values. The technique to determine AMSA values however is generally not instantaneous due to the need to sequentially sample and filter a large amount of electrocardiographic data and then perform multiple calculations. As such, AMSA is not recommended for routine use in the guideline for defibrillation management in adult cardiac arrest in the clinical setting in or out-of-hospital.

**[0013]** Establishing an accurate and rapid method to predict the success of defibrillation may have a substantial impact on the survival outcome of a patient. Several studies have demonstrated ETCO<sub>2</sub> values parallel changes in cardiac output, CoPP and myocardial perfusion while AMSA calculations are associated with CoPP. Since both AMSA and ETCO<sub>2</sub> are indicated to correlate with CoPP during cardiac arrest, one aspect of the disclosure is that ETCO<sub>2</sub> would reflect AMSA values during VF and CPR based upon the differences in flow as a consequence of the different methods of CPR. This association may provide a simple noninvasive means for medical practitioners to determine the optimal time for defibrillation. The present disclosure demonstrates a correlation between the parameters of ETCO<sub>2</sub> and AMSA. Specifically, three CPR methods, each generating a different level of perfusion, are utilized to establish the association between ETCO<sub>2</sub> and AMSA.

**[0014]** For example, FIG. 1 shows blood flow during CPR in the left ventricle and brain (porcine VF model) using a standard CPR procedure (STD CPR), a standard CPR procedure using an impedance threshold device (STD CPR+ITD), and an active compression-decompression CPR procedure using an impedance threshold device (ACD CPR+ITD). As shown in FIG. 1, magnitude of blood flow increases in order of: STD CPR (leftmost bar); STD CPR+ITD (middle bar); and ACD CPR+ITD (rightmost bar).

**[0015]** FIG. 2 shows detail of a swine model utilized to establish the association between ETCO<sub>2</sub> and AMSA. Twelve female farm pigs (32±1 kg) pigs (domestic cross-breed) were fasted overnight. They were sedated with 10 ml

(100 mg/ml) of intramuscular ketamine HCl (Ketaset, Fort Dodge Animal Health, Fort Dodge, Iowa). An intravenous bolus of propofol (PropoFlo, Abbott Laboratories, North Chicago, Ill.) (2-3 mg/kg) was given via a lateral ear vein and then infused at a rate of 160-200 .mu.g/kg/min for the remainder of the preparatory phase. The animals were intubated with a 7.5 mm cuffed French endotracheal tube inflated to prevent air leaks. Positive pressure, volume control ventilation with a tidal volume of 10 ml/kg and room air was delivered with a NarkoMed 4A (North American Drager) ventilator. The respiratory rate was adjusted (average  $12 \pm 2$  bpm) to keep oxygen saturation above 96% and  $\text{ETCO}_2$  between 38-42 mmHg. While in a ventral recumbent position, an intracranial bolt was inserted into the animal's parietal lobe to measure intracranial pressure using a 3.5 French micromanometer pressure transducer (Miko-Tip Transducer, Millar Instruments, Inc., Houston, Tex.). The animals were then placed supine. The left femoral artery and left external jugular vein were cannulated using a modified Seldinger percutaneous technique. Central aortic blood pressures were measured continuously via a micromanometer-tipped Millar catheter placed in the chest cavity at the level of origin of the thoracic descending aorta. Central venous blood pressures were measured via a micromanometer-tipped Millar catheter placed in the superior vena cava, approximately 2 cm above the right atrium. Right atrial pressures were maintained between 5-7 mmHg during the preparatory phase. Carotid artery blood flows were measured using a bidirectional Doppler flow probe attached to the internal carotid artery (Transonic Systems, Ithaca, N.Y.). Surface ECG was also monitored continuously. A thermometer was placed in the rectum and body temperature maintained with a heating blanket between 37.0.degree. C. and 38.0.degree. C. during pre-study and post-ROSC phases. All data were or was digitized using a computer data analysis program (BIOPAC MP 150, BIOPAC Systems Inc., Calif.).  $\text{ETCO}_2$ , tidal volume, and arterial oxygen saturation were recorded with a  $\text{CO}_2$ SMO Plus (Novamatrix Medical Systems, Wallingford, Conn.).

**[0016]** Following preparation, the animals were positioned for CPR and pre-arrest hemodynamic variables were measured. Ventricular fibrillation was induced in the anesthetized animal with application of a 50 Hz, 7.5 V AC electrical current through an electrophysiology catheter to the endocardial surface of the right ventricle. Propofol anesthesia was decreased to a rate of 100 .mu.g/kg/min and remained at this level during CPR. After 6 minutes of untreated cardiac arrest, mechanical CPR via a pneumatic piston attached to a compression pad was initiated. Chest compressions were performed with a rate of 100/min and a depth of 25% of the anteroposterior diameter as previously described. All animals were ventilated during CPR with supplemental oxygen (2 LPM) with a bag-valve resuscitator at a compression to ventilation ratio of 10:1 and a tidal volume of 10 ml/kg. As shown in FIG. 2, CPR was performed for a total of 9 minutes; 3 minutes of STD CPR, 3 minutes of STD CPR+impedance threshold device (ITD) (ResQPOD, Advanced Circulatory Systems Inc., Roseville, Minn., USA), and 3 minutes of active compression decompression (ACD) CPR+ITD. The transition from one method of CPR to the next was made in an uninterrupted manner.

ACD CPR was performed using a suction cup attached to the pneumatic piston as previously described. After the 9 minutes of CPR, epinephrine (40 .mu.g/Kg) was administered intravenously and 1 minute later the pigs were defibrillated with up to 3 additional sequential 200 Joule transthoracic biphasic shocks. Following successful resuscitation and one hour of observation, the animal was given a bolus of propofol (100 mg) and euthanized with a bolus intravenous injection of 10M KCl (30 mg/Kg).

**[0017]** As part of data analysis, the electrocardiographic (ECG) signal was sampled at 300 Hz and stored in 1.6 second increments such that each 4 second wavelet was processed at intervals of 1.6 seconds. The ECG signal was filtered between 3 and 30 Hz to minimize low frequency artifacts produced by precordial compression and to exclude the electrical interference of ambient noise at frequencies greater than 48 Hz. Analog ECG signals were digitized and converted from a time domain to a frequency domain by fast Fourier transformation via a computer data analysis program (BIOPAC). Utilizing MATLAB 5.1 software (Mathworks Inc., Natick, Mass.), the sum of individual amplitudes and frequencies resulted in the amplitude spectrum area (i.e., AMSA). Power spectrums for the VF waveform were generated the same way.

**[0018]** The mean AMSA for each pig for each intervention was used for the analysis. The mean values for all hemodynamic parameters extracted from multiple 4 second intervals obtained contemporaneously with the AMSA data were measured and used for future analysis. All values with a non-normal distribution are expressed as Median (25:75 percentiles). A Friedman statistical test was conducted to analyze  $\text{ETCO}_2$ , AMSA, the calculated coronary and cerebral perfusion pressure, aortic systolic, diastolic and mean pressure, right atrial pressure and intracranial pressure during the three CPR methods. Coronary perfusion pressures were determined by the difference between the diastolic aortic pressure and diastolic right atrial pressure during each CPR intervention. Cerebral perfusion pressures were determined by taking the difference between the aortic pressure and the intracranial pressure. Spearman correlation and Friedman tests were used to analyze the correlation between the different hemodynamic parameters. A Bland and Altman assessment was used to compare  $\text{ETCO}_2$  and AMSA values with a range of agreement defined as mean bias  $\pm 1.96$  SD. P values of  $<0.05$  were considered statistically significant. Statistical analyses were performed with SPSS® Statistics 17.0 (IBM Corporation, Somers, N.Y., USA).

**[0019]** In review of results, it was found that there were significant differences in the  $\text{ETCO}_2$ , AMSA, coronary perfusion pressure, cerebral perfusion pressure, systolic aortic pressure, mean aortic pressure, mean right atrial pressure and mean intracranial pressure based upon the method of CPR used. The key perfusion parameters were lowest with STD CPR, increased with STD CPR+ITD, and were highest with ACD CPR+ITD, as shown in Table 1:

TABLE 1

|           | ETCO <sub>2</sub> | AMSA             | Ao sys           | Ao dia         | Ao mean          | RA mean          | ICP mean        | CePP           | CoPP           | CBF         |
|-----------|-------------------|------------------|------------------|----------------|------------------|------------------|-----------------|----------------|----------------|-------------|
| STD       | 5.7               | 31.1             | 30.7             | 9.5            | 20.2             | 12.6             | 18.3            | 2.8            | 8.4            | 25          |
| CPR       | (4.5;<br>7.9)*    | (26.9;<br>39.4)* | (28.3;<br>35.2)* | (8.4;<br>12.1) | (18.2;<br>22.4)* | (11.4;<br>15.7)* | (14.8;<br>22)*  | (1.4;<br>8.1)* | (6.1;<br>10)*  | (14;<br>36) |
| STD       | 15.2              | 39.7             | 37.7             | 10.5           | 22.9             | 15.5             | 19.6            | 5.7            | 10.6           | 24          |
| CPR + ITD | (13.9;<br>18.4)   | (29.9;<br>45.8)  | (33;<br>64.7)    | (8.9;<br>19.4) | (22;<br>39.9)    | (13.4;<br>27.5)  | (16.2;<br>23.7) | (3.2;<br>14.8) | (7.9;<br>13.3) | (14;<br>29) |
| ACD       | 20.5              | 45.5             | 41.9             | 11.5           | 25.9             | 16.6             | 18.4            | 7.6            | 13.3           | 27          |
| CPR + ITD | (16.5;<br>21.5)   | (31.5;<br>50.8)  | (37;<br>59.9)    | (7.6;<br>18)   | (23.7;<br>34.1)  | (14.1;<br>22.3)  | (15.2;<br>22.9) | (4.9;<br>17)   | (7.9;<br>19.7) | (19;<br>45) |

Median (25; 75 percentile); hemodynamic parameter using the three different cardiopulmonary resuscitation techniques.

Ao sys: systolic aortic pressure;

Ao dia: diastolic aortic pressure;

Ao mean: mean aortic pressure;

RA mean: mean right atrial pressure;

ICP mean: mean intracranial pressure;

CePP: cerebral perfusion pressure;

CoPP: Coronary perfusion pressure;

ETCO<sub>2</sub>: end tidal CO<sub>2</sub> (mmHg);

AMSA: amplitude spectral area (mV-Hz);

CBF: Mean carotid blood flow (ml/min);

\*p = 0.001 STD CPR < STD CPR + ITD < ACD CPR + ITD (Friedman statistical test).

The data of Table 1 is shown graphically in FIG. 3, STD CPR (leftmost bar); STD CPR+ITD (middle bar); and ACD CPR+ITD (rightmost bar).

[0020] The power spectrum for the VF waveform also changed significantly based upon the method of CPR. FIG. 4 shows a representative spectrum from one pig during each of the 3 methods of CPR, STD CPR (frontmost curve or trend); STD CPR+ITD (middle curve or trend); and ACD CPR+ITD (rearmost curve or trend). There was a pro-

nounced increase in the high frequency signal in this representative study and when the respective values for all animals were averaged.

[0021] Further analysis demonstrated a correlation between AMSA and ETCO<sub>2</sub> (r=0.374, p=0.025) and a correlation between AMSA and key hemodynamic parameters (coronary perfusion pressure, cerebral perfusion pressure, aortic systolic, diastolic and mean pressure) (p<0.05), as shown in Table 2:

TABLE 2

|                   | AMSA   | Ao sys | Ao dia | Ao mean | CePP   | CoPP   | CBF    |
|-------------------|--------|--------|--------|---------|--------|--------|--------|
| ETCO <sub>2</sub> | 0.374* | 0.709* | 0.315  | 0.723*  | 0.526* | 0.340* | 0.295  |
|                   | 0.025  | <0.001 | 0.061  | <0.001  | 0.001  | 0.043  | 0.08   |
| AMSA              |        | 0.541* | 0.487* | 0.612*  | 0.217  | 0.185  | 0.639* |
|                   |        | 0.001  | 0.003  | <0.001  | 0.203  | 0.281  | <0.001 |
| Ao sys            |        |        | 0.611* | 0.953*  | 0.825* | 0.514* | 0.567* |
|                   |        |        | <0.001 | <0.001  | <0.001 | 0.001  | <0.001 |
| Ao dia            |        |        |        | 0.709*  | 0.499* | 0.514* | 0.411* |
|                   |        |        |        | <0.001  | 0.002  | 0.001  | 0.006  |
| Ao mean           |        |        |        |         | 0.77*  | 0.575* | 0.597* |
|                   |        |        |        |         | <0.001 | <0.001 | <0.001 |
| CePP              |        |        |        |         |        | 0.503* | 0.373* |
|                   |        |        |        |         |        | 0.002  | <0.001 |

Ao Ao Ao AMSA sys dia mean CePP CoPP CBF ETCO<sub>2</sub> 0.374\* 0.709\* 0.315 0.723\* 0.526\* 0.340\* 0.295 0.025 <0.001 0.061 <0.001 0.001 0.043 0.08 AMSA 0.541\* 0.487\* 0.612\* 0.217 0.185 0.639\* 0.001 0.003 <0.001 0.203 0.281 <0.001 Ao 0.611\* 0.953\* 0.825\* 0.514\* 0.567\* sys <0.001 <0.001 <0.001 <0.001 Ao 0.709\* 0.499\* 0.514\* 0.411\* dia <0.001 0.002 0.001 0.006 Ao 0.77\* 0.575\* 0.597\* mean <0.001 <0.001 <0.001 CePP 0.503\* 0.373\* 0.002 <0.001

Correlation between the different hemodynamic parameter, rs and p, \*correlation is significant.

Ao sys: systolic aortic pressure;

Ao dia: diastolic aortic pressure;

Ao mean: mean aortic pressure;

RA mean: mean right atrial pressure;

ICP mean: mean intracranial pressure;

CePP: cerebral perfusion pressure;

CoPP: Coronary perfusion pressure;

ETCO<sub>2</sub>: end tidal CO<sub>2</sub> (mmHg);

AMSA: amplitude spectral area (mV-Hz);

CBF: Mean carotid blood flow (ml/min). Those are r.

FIG. 5 demonstrates the correlation between AMSA and  $\text{ETCO}_2$ : STD CPR (diamond); STD CPR+ITD (square); and ACD CPR+ITD (triangle).

[0022] The Bland-Altman analysis indicated the 95% limits of agreement between AMSA and  $\text{ETCO}_2$  ranged from  $-21.4$  to  $-33.5$ . This is shown graphically in FIG. 6: STD CPR (diamond); STD CPR+ITD (square); and ACD CPR+ITD (triangle). These study results indicate a strong association between AMSA and  $\text{ETCO}_2$ .

[0023] Research has conventionally focused on finding a non-invasive method to predict the success of defibrillation with the hope of having a substantial impact on the survival outcome of patients. AMSA has been reported to provide an 86% positive and an 85% negative predictive value, respectively for a threshold value at  $21 \text{ mV}\times\text{Hz}$ . However AMSA values can be difficult to calculate in real-time and are not recommended for routine use in the guideline for defibrillation management in adult cardiac arrest in the clinical setting in or out-of-hospital. By contrast, continuous  $\text{ETCO}_2$  waveforms are readily obtainable and can be rapidly analyzed. Using three different methods of CPR to consistently vary different organ perfusion levels, a correlation between  $\text{ETCO}_2$  and AMSA is demonstrated. Because of this newly discovered correlation, techniques for using  $\text{ETCO}_2$  values, alone or in combination with AMSA values, to direct a caregivers are proposed as to when to apply a defibrillating shock. More specifically, if the measured  $\text{ETCO}_2$  values are within an acceptable range or near an acceptable value, an indication may be supplied to the caregiver as to when to apply a defibrillating shock.

[0024] FIG. 7 shows an example treatment system 700 in accordance with the present disclosure. The system 700 may include a facial mask 702 and a valve system 704. The valve system 704 may be coupled to a controller 706. In turn, the controller 706 may be used to control an impedance level of the valve system 704. The level of impedance may be varied based on measurements of physiological parameters, or using a programmed schedule of changes. The system 700 may include a wide variety of sensors and/or measuring devices to measure any of a number physiological parameters. Such sensors or measuring devices may be integrated within or coupled to the valve system 704, the facial mask 702, etc., or may be separate depending on implementation. An example of sensors and/or measuring devices may include a pressure transducer for taking pressure measurements (such as intrathoracic pressures, intracranial pressures, intraocular pressures), a flow rate measuring device for measuring the flow rate of air into or out of the lungs, or a  $\text{CO}_2$  sensor for measuring expired  $\text{CO}_2$ . Examples of other sensors or measuring devices include a heart rate sensor 708, a blood pressure sensor 710, and a temperature sensor 712. These sensors may also be coupled to the controller 706 so that measurements may be recorded. Further, it will be appreciated that other types of sensors and/or devices may be coupled to the controller 706 and may be used to implement defibrillation and measure various physiological parameters, such as bispectral index, oxygen saturation and/or blood levels of  $\text{O}_2$ , blood lactate, blood pH, tissue lactate, tissue pH, blood pressure, pressures within the heart, intrathoracic pressures, positive end expiratory pressure, respiratory rate, intracranial pressures, intraocular pressures, respiratory flow, oxygen delivery, temperature, end-tidal  $\text{CO}_2$ , tissue  $\text{CO}_2$ , cardiac output, and many others.

[0025] For example, ECG electrode(s) or sensor(s) 720 may also be coupled to the controller 706 so that measurements related to the electrical activity of an individual's heart may be monitored and recorded. Advantageously, this may allow for the acquisition and/or derivation of AMSA values of a particular individual during a CPR procedure, as discussed throughout the present disclosure. Additionally, a display screen 722 and one or more speakers 724 may be coupled to the controller 706 to provide a prompt to a rescuer, such as a prompt to "cue" a rescuer to defibrillate an individual while CPR is performed on the individual. Such a feature is discussed in further detail in connection with at least FIG. 8. Even further, one or more electrodes 726 may be coupled to the controller 706 to enable application of a defibrillation shock(s) either automatically (e.g., without direct user-input) or manually (e.g., in response to activation of a particular "button"). Still many other devices, sensors, etc., may be coupled to the controller 706 as needed or desired, to implement the various features or aspects of the present disclosure.

[0026] In some cases, the controller 706 may be used to control the valve system 704, to control any sensors or measuring devices, to record measurements, and to perform any comparisons. Alternatively, a set of computers and/or controllers may be used in combination to perform such tasks. This equipment may have appropriate processors, display screens, input and output devices, entry devices, memory or databases, software, and the like needed to operate the system 700. A variety of devices may also be coupled to controller to cause the person to artificially inspire. For example, such devices may comprise a ventilator 714, an iron lung cuirass device 716 or a phrenic nerve stimulator 718. The ventilator 714 may be configured to create a negative intrathoracic pressure within the person, or may be a high frequency ventilator capable of generating oscillations at about 200 to about 2000 per minute. Other embodiments are possible.

[0027] FIG. 8 shows an example computer system or device 800 in accordance with the present disclosure. An example of a computer system or device includes a medical device, a desktop computer, a laptop computer, a tablet computer, and/or any other type of machine configured for performing calculations. The example computer device 800 may be configured to perform and/or include instructions that, when executed, cause the computer system 800 to perform a method for providing a guide to determine when to defibrillate an individual using  $\text{ETCO}_2$  measurements alone. The example computer device 800 may be configured to perform and/or include instructions that, when executed, cause the computer system 800 to perform a method for providing a guide to determine when to defibrillate an individual using  $\text{ETCO}_2$  measurements and AMSA values. The particular trigger of when to provide the shock may be based on part on the correlation between the  $\text{ETCO}_2$  measurements and predetermined AMSA values, or may be determined empirically based on test data using  $\text{ETCO}_2$  measurements. It is thus contemplated that the example computer device 800 may be coupled to one or more sensors configured and arranged to acquire and/or operate on such measurements or data, itself have integrated therein one or more sensors configured and arranged to acquire and/or operate on such measurements or data, or any combination thereof.

**[0028]** Furthermore, it is contemplated that the example computer system **800** may include or comprise at least one of an audio speaker and a display monitor so as to provide at least one of an audio indication (e.g., a particular tone or series of tones such as a single or periodic or intermittent “beep,” a particular word such as a “go” or “defibrillate,” and etc.) and a visual indication (e.g., a particular colored screen or series of screens such as a “green” screen or periodically or intermittently “flashing” screens of one or more particular colors, a particular graphic such as a “go” or “defibrillate,” and etc.) so that a medical professional or other individual may be “cued” to defibrillate an individual during CPR as performed on the individual as discussed throughout the present disclosure. Such features may be embodied by the output device(s) **808** shown in FIG. **8** discussed further below.

**[0029]** The computer device **800** is shown comprising hardware elements that may be electrically coupled via a bus **802** (or may otherwise be in communication, as appropriate). The hardware elements may include a processing unit with one or more processors **804**, including without limitation one or more general-purpose processors and/or one or more special-purpose processors (such as digital signal processing chips, graphics acceleration processors, and/or the like); one or more input devices **806**, which may include without limitation a remote control, a mouse, a keyboard, and/or the like; and one or more output devices **808**, which may include without limitation, a video monitor or screen, an audio speaker, a printer, and/or the like.

**[0030]** The computer system **800** may further include (and/or be in communication with) one or more non-transitory storage devices **810**, which may comprise, without limitation, local and/or network accessible storage, and/or may include, without limitation, a disk drive, a drive array, an optical storage device, a solid-state storage device, such as a random access memory, and/or a read-only memory, which may be programmable, flash-updateable, and/or the like. Such storage devices may be configured to implement any appropriate data stores, including without limitation, various file systems, database structures, and/or the like.

**[0031]** The computer device **800** might also include a communications subsystem **812**, which may include without limitation a modem, a network card (wireless or wired), an infrared communication device, a wireless communication device, and/or a chipset, such as a Bluetooth™ device, an 802.11 device, a WiFi device, a WiMax device, hardwired and/or wireless communication facilities, and/or the like. The communications subsystem **812** may permit data to be exchanged with a private and/or non-private network, other computer systems, and/or any other devices described herein. In many embodiments, the computer system **800** may further comprise a working memory **814**, which may include a random access memory and/or a read-only memory device, as described above.

**[0032]** The computer device **800** also may comprise software elements, shown as being currently located within the working memory **814**, including an operating system **816**, device drivers, executable libraries, and/or other code, such as one or more application programs **818**, which may comprise computer programs provided by various embodiments, and/or may be designed to implement methods, and/or configure systems, provided by other embodiments, as described herein. By way of example, one or more procedures described with respect to the method(s) dis-

cussed above, and/or system components might be implemented as code and/or instructions executable by a computer (and/or a processor within a computer); in an aspect, then, such code and/or instructions may be used to configure and/or adapt a general purpose computer (or other device) to perform one or more operations in accordance with the described methods.

**[0033]** A set of these instructions and/or code might be stored on a non-transitory computer-readable storage medium, such as the storage device(s) **810** described above. In some cases, the storage medium might be incorporated within a computer system, such as computer system **800**.

**[0034]** In other embodiments, the storage medium might be separate from a computer system (e.g., a removable medium, such as flash memory), and/or provided in an installation package, such that the storage medium may be used to program, configure, and/or adapt a general purpose computer with the instructions/code stored thereon. These instructions might take the form of executable code, which is executable by the computer device **800** and/or might take the form of source and/or installable code, which, upon compilation and/or installation on the computer system **800** (e.g., using any of a variety of generally available compilers, installation programs, compression/decompression utilities, etc.), then takes the form of executable code.

**[0035]** It will be apparent to those skilled in the art that substantial variations may be made in accordance with specific requirements. For example, customized hardware might also be used, and/or particular elements might be implemented in hardware, software (including portable software, such as applets, etc.), or both. Further, connection to other computing devices such as network input/output devices may be employed.

**[0036]** As mentioned above, in one aspect, some embodiments may employ a computer system (such as the computer device **800**) to perform methods in accordance with various embodiments of the invention. According to a set of embodiments, some or all of the procedures of such methods are performed by the computer system **800** in response to processor **804** executing one or more sequences of one or more instructions (which might be incorporated into the operating system **816** and/or other code, such as an application program **818**) contained in the working memory **814**.

**[0037]** Such instructions may be read into the working memory **814** from another computer-readable medium, such as one or more of the storage device(s) **810**. Merely by way of example, execution of the sequences of instructions contained in the working memory **814** may cause the processor(s) **804** to perform one or more procedures of the methods described herein.

**[0038]** The terms “machine-readable medium” and “computer-readable medium,” as used herein, may refer to any medium that participates in providing data that causes a machine to operate in a specific fashion. In an embodiment implemented using the computer device **800**, various computer-readable media might be involved in providing instructions/code to processor(s) **804** for execution and/or might be used to store and/or carry such instructions/code. In many implementations, a computer-readable medium is a physical and/or tangible storage medium. Such a medium may take the form of a non-volatile media or volatile media. Non-volatile media may include, for example, optical and/or magnetic disks, such as the storage device(s) **810**. Volatile

media may include, without limitation, dynamic memory, such as the working memory **814**.

**[0039]** Example forms of physical and/or tangible computer-readable media may include a floppy disk, a flexible disk, hard disk, magnetic tape, or any other magnetic medium, a CD-ROM, any other optical medium, a RAM, a PROM, EPROM, a FLASH-EPROM, any other memory chip or cartridge, or any other medium from which a computer may read instructions and/or code.

**[0040]** Various forms of computer-readable media may be involved in carrying one or more sequences of one or more instructions to the processor(s) **804** for execution. By way of example, the instructions may initially be carried on a magnetic disk and/or optical disc of a remote computer. A remote computer might load the instructions into its dynamic memory and send the instructions as signals over a transmission medium to be received and/or executed by the computer system **800**.

**[0041]** The communications subsystem **812** (and/or components thereof) generally will receive signals, and the bus **802** then might carry the signals (and/or the data, instructions, etc. carried by the signals) to the working memory **814**, from which the processor(s) **804** retrieves and executes the instructions. The instructions received by the working memory **814** may optionally be stored on a non-transitory storage device **810** either before or after execution by the processor(s) **804**.

**[0042]** As may be understood from the foregoing discussion in connection with the drawings, it is contemplated that  $\text{ETCO}_2$  measurements may be used alone as a guide to determine when to defibrillate an individual. Alternatively,  $\text{ETCO}_2$  measurements may be used in combination with amplitude spectral area measurements as a guide to determine when to defibrillate an individual.

**[0043]** In particular, in some aspects, a computer-implemented method may include or comprise obtaining, by a computing or measuring system, an  $\text{ETCO}_2$  measurement of an individual during a CPR procedure performed on the individual. The method may further include or comprise comparing, by the computing system, a particular  $\text{ETCO}_2$  value derived from the  $\text{ETCO}_2$  measurement to a predetermined threshold value. The method may further include or comprise providing, by the computing system based on the comparing, a perceivable indication that designates a time to deliver a defibrillation shock to the individual. Further, the computing system may, in some embodiments, use a change from one time point to the next or another, in  $\text{ETCO}_2$  measurements, to determine the time to delivery of a defibrillation shock. The  $\text{ETCO}_2$  measurements could include peak and/or trough  $\text{ETCO}_2$  values, mean values, or  $\text{ETCO}_2$  waveform characteristics which are affected by the amount of blood circulating or in circulation during CPR in the individual.

**[0044]** Additionally, or alternatively, the method may include or comprise providing the indication when the particular  $\text{ETCO}_2$  value is less than or equal to the predetermined threshold value. For example, when  $\text{ETCO}_2$  levels are persistently less than 10 mmHg, then the chances for a successful defibrillation may be considered to be extremely low and such information may be used by the computing system to determine that a defibrillatory shock should not be delivered at that time. Additionally, or alternatively, the method may include or comprise providing the indication

when the particular  $\text{ETCO}_2$  value is greater than or equal to the predetermined threshold value.

**[0045]** Additionally, or alternatively, the method may include or comprise providing, by the computing system based on the comparison, at least one of an audio indication and a visual indication that designates the time to deliver the defibrillation shock to the individual. The visual indication could be provided in the form of an absolute number or a graph of changes in  $\text{ETCO}_2$  or a derivative of  $\text{ETCO}_2$  over time, with an indication for the threshold value needed before a shock should be delivered.

**[0046]** Additionally, or alternatively, the method may include or comprise obtaining an electrocardiogram (ECG) measurement of the individual during the CPR procedure; deriving from the ECG measurement an amplitude spectral area value; and providing the indication that designates the time to deliver the defibrillation shock to the individual based upon the amplitude spectrum area value and the comparison of the  $\text{ETCO}_2$  value to the predetermined threshold value. For example, both AMSA and  $\text{ETCO}_2$  values would have to be at a threshold value before a shock is delivered, thereby providing the greatest likelihood for a successful defibrillation and survival. In this manner, the computing system may take into account both measurements before advising or triggering a defibrillatory shock. Other potential combinations of these two distinctly different physiological signals to provide a greater degree of predictive certainty of defibrillation success or failure include the value obtained by multiplying, or performing another mathematical operation, the  $\text{ETCO}_2$  and AMSA values together to achieve a number that would provide an indicator that defibrillation would be successful.

**[0047]** In some aspects, a method may include or comprise performing a cardiopulmonary resuscitation (CPR) procedure on an individual; and delivering a defibrillation shock to the individual at a particular time based upon an indication provided by a computing system when a particular end-tidal carbon dioxide ( $\text{ETCO}_2$ ) value derived from an  $\text{ETCO}_2$  measurement of the individual during the CPR procedure is determined by the computing system as less than or greater than a predetermined threshold value. In some embodiments, once the rescuer observes the indication, then they would deliver the defibrillatory shock within the next 30-60 seconds. In cases where the shock is not successful, a follow-up  $\text{ETCO}_2$  value could be used to determine if an additional 1-2 minutes of CPR is needed or whether the rescuer should charge the defibrillator and immediately deliver another shock. Thus, the post shock  $\text{ETCO}_2$  value could be used to help determine the timing of follow up shocks if the first one is not successful. The computing system may adjust for the failed shock such that the next shock would not be advised unless the  $\text{ETCO}_2$  values were higher, for example, 10% higher than those measured prior to the first shock.

**[0048]** Additionally, or alternatively, the method may include or comprise performing an intrathoracic pressure regulation procedure or a reperfusion injury protection procedure at or during the CPR procedure. Additionally, or alternatively, the method may include or comprise periodically extracting respiratory gases from the airway of the individual to create an intrathoracic vacuum that lowers pressure in the thorax to at least one of: enhance the flow of blood to the heart of the individual; lower intracranial pressures of the individual; and enhance cerebral perfusion

pressures of the individual. Additionally, or alternatively, the method may include or comprise preventing air from at least temporarily entering the lungs of the individual during at least a portion of a relaxation or decompression phase of the CPR procedure to create an intrathoracic vacuum that lowers pressure in the thorax to at least one of: enhance flow of blood to the heart of the particular individual; lower intracranial pressures of the particular individual; and enhance cerebral perfusion pressures of the individual. The methods and devices used to perform CPR could include manual closed chest CPR, CPR with an active compression decompression device, and such CPR methods could be used together with an impedance threshold device to transiently impede inspiratory flow during the recoil phase of CPR or an intrathoracic pressure regulatory to actively extract gases from the lungs.

**[0049]** Additionally, or alternatively, the method may include or comprise performing a standard CPR procedure on the individual. Additionally, or alternatively, the method may include or comprise performing a stutter CPR procedure on the individual to achieve some degree of reperfusion injury protection. Additionally, or alternatively, the method may include or comprise performing an active compression-decompression CPR procedure on the individual. Additionally, or alternatively, the method may include or comprise positioning a mechanical CPR device relative to the chest of the individual; and activating the mechanical CPR device to perform a mechanized CPR procedure on the individual. Such CPR devices could include, but would not be limited to, a LUCAS device (Physio-control, Redmond, Wash.), the Zoll Autopulse (Chelmsford, Mass.), the Michigan Instrument Thumper (Grand Rapids, Mich.).

**[0050]** Additionally, or alternatively, the method may include or comprise delivering the defibrillation shock to the individual upon perception of the indication provided by the computing system at the particular time based upon an amplitude spectrum area value of the individual as derived from a measurement during the CPR procedure and when the particular ETCO<sub>2</sub> value is determined as less than or equal, or greater than or equal to the predetermined threshold value. Additionally, or alternatively, the method may include or comprise delivering the defibrillation shock to the individual upon perception of at least one of an audio indication and a visual indication provided by the computing system.

**[0051]** In some aspects, a system, device, or apparatus may include or comprise a first device that monitors concentration of carbon dioxide in respiratory gases of an individual at least during a cardiopulmonary resuscitation (CPR) procedure performed on the individual; a second device that compares a particular end-tidal carbon dioxide value derived from the concentration of carbon dioxide in respiratory gases of the individual to a predetermined threshold value; and a third device that provides based on the comparison a perceivable indication that designates a time to deliver a defibrillation shock to the individual. The second device may be used with the third device to determine the optimal time to deliver the shock and, if the first shock fails, may use the same or different logic to determine the time to deliver additional shocks.

**[0052]** Additionally, or alternatively, the system, device, or apparatus may include or comprise an electroencephalogram (EEG) sensor that measures an EEG signal of the individual at least during the CPR procedure performed on

the individual, wherein the second device derives an amplitude spectrum area value from the EEG signal, and the third device provides the perceivable indication based upon the amplitude spectrum area value and the comparison of the particular end-tidal carbon dioxide value to the predetermined threshold value. Additionally, or alternatively, the system, device, or apparatus may include or comprise a circulation enhancement device that enhances circulation of the individual at least during the CPR procedure performed on the individual.

**[0053]** The methods, systems, and devices discussed above are examples. Various configurations may omit, substitute, or add various method steps or procedures, or system components as appropriate. For instance, in alternative configurations, the methods may be performed in an order different from that described, and/or various stages may be added, omitted, and/or combined. Also, features described with respect to certain configurations may be combined in various other configurations. Different aspects and elements of the configurations may be combined in a similar manner. Also, technology evolves and, thus, many of the elements are examples and do not limit the scope of the disclosure or claims.

**[0054]** Specific details are given in the description to provide a thorough understanding of example configurations (including implementations). However, configurations may be practiced without these specific details. For example, well-known circuits, processes, algorithms, structures, and techniques have been shown without unnecessary detail in order to avoid obscuring the configurations. This description provides example configurations only, and does not limit the scope, applicability, or configurations of the claims. Rather, the preceding description of the configurations will provide those skilled in the art with an enabling description for implementing described techniques. Various changes may be made in the function and arrangement of elements without departing from the spirit or scope of the disclosure.

**[0055]** Also, configurations may be described as a process which is depicted as a flow diagram or block diagram. Although each may describe the operations as a sequential process, many of the operations may be performed in parallel or concurrently. In addition, the order of the operations may be rearranged. A process may have additional steps not included in the figure. Furthermore, examples of the methods may be implemented by hardware, software, firmware, middleware, microcode, hardware description languages, or any combination thereof. When implemented in software, firmware, middleware, or microcode, the program code or code segments to perform the necessary tasks may be stored in a non-transitory computer-readable medium such as a storage medium. Processors may perform the described tasks.

**[0056]** Furthermore, the example embodiments described herein may be implemented as logical operations in a computing device in a networked computing system environment. The logical operations may be implemented as: (i) a sequence of computer implemented instructions, steps, or program modules running on a computing device; and (ii) interconnected logic or hardware modules running within a computing device.

**[0057]** Although the subject matter has been described in language specific to structural features and/or methodological acts, it is to be understood that the subject matter defined in the appended claims is not necessarily limited to the

specific features or acts described above. Rather, the specific features and acts described above are disclosed as example forms of implementing the claims.

1. A method of guiding defibrillation therapy of an individual during resuscitation, comprising:

obtaining, by a defibrillation system, signals representing a non-invasive end-tidal carbon dioxide (ETCO<sub>2</sub>) measurement of the individual during the resuscitation;

obtaining, by the defibrillation system, signals representing a non-invasive electrocardiogram (ECG) measurement of the individual during the resuscitation;

analyzing the signals representing the ETCO<sub>2</sub> measurement and the signals representing the ECG measurement to determine whether to deliver a defibrillation shock to the individual; and

providing, by the defibrillation system, a perceivable indication that designates a time to deliver a defibrillation shock to the individual, based upon the analyzed signals representing the ETCO<sub>2</sub> measurements and the analyzed signals representing the ECG measurement.

2. The method of claim 1,

wherein the perceivable indication is provided when the ETCO<sub>2</sub> measurement is less than or equal to a predetermined threshold value.

3. The method of claim 1,

wherein the perceivable indication is provided when the ETCO<sub>2</sub> measurement is greater than or equal to a predetermined threshold value.

4. The method of claim 1, wherein the perceivable indication is a visual indication that designates the time to deliver the defibrillation shock.

5. The method of claim 1, wherein the step of analyzing the signals representing the ECG measurement comprises deriving an amplitude spectrum area value, and wherein the amplitude spectrum area value provides an indication of the likelihood that the defibrillation shock will be successful.

6. A method, comprising:

performing a cardiopulmonary resuscitation (CPR) procedure on an individual; and

delivering a defibrillation shock to the individual at a particular time based upon an indication provided by a computing system based on when a particular end-tidal carbon dioxide (ETCO<sub>2</sub>) value derived from a non-invasive ETCO<sub>2</sub> measurement of the individual during the CPR procedure is determined by the computing system as less than or greater than a predetermined threshold value and on electrocardiogram (ECG) value derived from a non-invasive ECG measurement.

7-13. (canceled)

14. The method of claim 6, further comprising:

delivering the defibrillation shock to the individual upon perception of the indication provided by the computing system at the particular time based upon an amplitude spectrum area value derived from the ECG measurement and when the particular ETCO<sub>2</sub> value is determined as less than or equal to the predetermined threshold value.

15. The method of claim 6, further comprising:

delivering the defibrillation shock to the individual upon perception of the indication provided by the computing system at the particular time based upon an amplitude spectrum area value derived from the ECG measure-

ment and when the particular ETCO<sub>2</sub> value is determined as greater than or equal to the predetermined threshold value.

16. The method of claim 6, wherein an amplitude spectrum area value derived from the ECG measurement provides an indication of the likelihood that the defibrillation shock will be successful.

17-22. (canceled)

23. The method of claim 1, wherein the perceivable indication is provided when the ETCO<sub>2</sub> measurement changes from a previously obtained measurement.

24. The method of claim 1, wherein the perceivable indication is provided when either:

the ETCO<sub>2</sub> measurement and the ECG measurement are less than or equal to a predetermined threshold value; or

the ETCO<sub>2</sub> measurement and the ECG measurement are greater than or equal to a predetermined threshold value.

25. The method of claim 6, wherein the indication is provided when either:

the ETCO<sub>2</sub> measurement is less than or equal to a predetermined threshold value; or

the ETCO<sub>2</sub> measurement is greater than or equal to a predetermined threshold value.

26. The method of claim 6, wherein the indication is provided when the ETCO<sub>2</sub> measurement changes from a previously obtained measurement.

27. A defibrillation apparatus for guiding defibrillation therapy of an individual during resuscitation, comprising:

a first non-invasive sensor that acquires signals representing an end-tidal carbon dioxide (ETCO<sub>2</sub>) measurement of the individual during the resuscitation;

a second non-invasive sensor that acquires signals representing an electrocardiogram (ECG) measurement of the individual during the resuscitation; and

a processor in communication with the sensors and configured to:

analyze the signals representing the ETCO<sub>2</sub> measurement and the signals representing the ECG measurement to determine whether to deliver a defibrillation shock to the individual, and

provide a perceivable indication that designates whether to deliver the defibrillation shock to the individual based upon the analyzed signals representing the ETCO<sub>2</sub> measurements and the analyzed signals representing the ECG measurement.

28. The apparatus of claim 27, further comprising one or more electrodes in communication with the processor for delivering a defibrillation shock.

29. The apparatus of claim 28, wherein the processor controls delivery of the defibrillation shock, and wherein the processor automatically delivers a defibrillation shock to the individual at the designated time.

30. The apparatus of claim 27, wherein the step of analyzing the signals representing the ECG measurement comprises deriving an amplitude spectrum area value, and wherein the amplitude spectrum area value provides an indication of the likelihood that the defibrillation shock will be successful.

31. The apparatus of claim 27, wherein the perceivable indication is provided when either:

the ETCO<sub>2</sub> measurement is less than or equal to a predetermined threshold value, or

the  $\text{ETCO}_2$  measurement is greater than or equal to a predetermined threshold value.

**32.** The apparatus of claim **27**, wherein the perceivable indication is a visual indication that designates the time to deliver the defibrillation shock.

**33.** The apparatus of claim **27**, wherein the perceivable indication is provided when the  $\text{ETCO}_2$  measurement changes from a previously obtained measurement.

**34.** The apparatus of claim **27**, wherein the perceivable indication is provided when either:

the  $\text{ETCO}_2$  measurement and the ECG measurement are less than or equal to a predetermined threshold value;  
or

the  $\text{ETCO}_2$  measurement and the ECG measurement are greater than or equal to a predetermined threshold value.

\* \* \* \* \*

|                |   |         |            |
|----------------|---|---------|------------|
| 专利名称(译)        | 呼气末二氧化碳和幅度谱区作为冠状动脉灌注压的非侵入性标志物   |         |            |
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| [标]申请(专利权)人(译) | RESQSYST  |         |            |
| 申请(专利权)人(译)    | RESQSYSTEMS INC.  |         |            |
| 当前申请(专利权)人(译)  | RESQSYSTEMS INC.  |         |            |
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摘要(译)

呼气末二氧化碳 (ETCO<sub>2</sub>) 测量可单独用作确定何时对个体进行除颤的指导。或者, ETCO<sub>2</sub> 测量可以与幅度谱面积测量结合使用, 作为确定何时对个体进行除颤的指导。

