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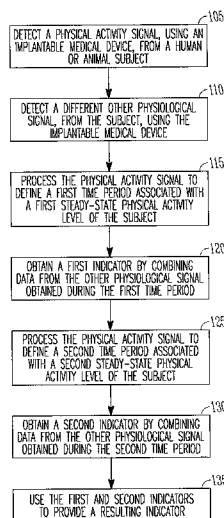
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- (71) **Applicant (for all designated States except US):** **CARDIAC PACEMAKERS, INC.** [US/US]; 4100 Hamline Avenue North, St. Paul, Minnesota 55112-5798 (US).
- (72) **Inventors; and**
- (75) **Inventors/Applicants (for US only):** **BECK, Kenneth** [US/US]; 1908 Bluestem Lane, Shoreview, Minnesota 55126 (US). **BAKER, Lemont** [US/US]; 400 North First Street, Apt. 506, Minneapolis, Minnesota 55401 (US). **HOPPER, Donald** [US/US]; 11761 99th Avenue North, Maple Grove, Minnesota 55369 (US).
- (74) **Agents:** **CLISE, Timothy, B.** et al.; Schwegman, Lundberg, Woessner & Kluth, P.O. Box 2938, Minneapolis, Minnesota 55402 (US).
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(54) **Title:** MONITORING PHYSIOLOGICAL RESPONSES TO STEADY STATE ACTIVITY



(57) **Abstract:** Systems and methods monitor physiological responses to steady state activity. In an example, a physical activity signal is detected from a human or animal subject using an implantable medical device. A different, other physiological signal is also detected from the subject using the implantable medical device. The physical activity signal is processed to define first and second time periods associated with first and second steady-state physical activity levels of the subject. A first indicator is obtained by combining data from the other physiological signal obtained during the first time period. A second indicator is obtained by combining data from the other physiological signal obtained during the second time period. The first and second indicators are used provide a resulting indicator.

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MONITORING PHYSIOLOGICAL RESPONSES TO STEADY STATE ACTIVITY

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CLAIM OF PRIORITY

Benefit of priority is hereby claimed to U.S. Patent Application Serial
Number 11/184,327, filed on July 19, 2005, which application is herein
10 incorporated by reference.

TECHNICAL FIELD

This patent document pertains generally to measuring physiological
activity, and more particularly, but not by way of limitation, to methods and
15 apparatus for monitoring physiological responses to steady state activity.

BACKGROUND

Implantable devices such as pacers and defibrillators detect and process
physiological data. For example, some devices detect an intrinsic electrical heart
20 signal using one or more electrodes on a lead that is coupled to the device.
Pacers, for example, use sensed data to adjust the target heart rate of a patient.
Defibrillators analyze heart activity to assess whether an antitachyarrhythmia
therapy is needed. Other parameters such as blood pressure are also detectable
using implantable sensors.

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SUMMARY

An example method includes detecting a physical activity signal, using
an implantable medical device, from a human or animal subject, detecting a
different other physiological signal, from the subject, using the implantable
30 medical device. The method further includes processing the physical activity
signal to define a first time period associated with a first steady-state physical
activity level of the subject, including identifying for the first time period a first
beginning time at which the physical activity of the subject is deemed to be at
steady state at the first steady-state physical activity level, and a first ending time
35 at which the subject leaves the first steady-state physical activity level. The

method further includes processing the physical activity signal to define a second time period associated with a second steady-state physical activity level of the subject, including identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at the
5 second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level. The method also includes obtaining a first indicator by combining data from the other physiological signal obtained during the first time period, obtaining a second indicator by combining data from the other physiological signal obtained during
10 the second time period, and using the first and second indicators to provide a resulting indicator.

Another example machine-assisted method comprising detecting a physical activity signal, using an implantable medical device, from a human or animal subject, the physical activity signal falling within an activity range
15 divided into activity bins, and contemporaneously detecting a different other physiological signal, from the subject, using the implantable medical device. The method further includes processing the physical activity signal to define a first time period associated with a first steady-state physical activity level of the subject, including identifying for the first time period a first beginning time at
20 which the physical activity of the subject is deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level, the first steady-state physical activity level corresponding to an activity bin. The method also includes processing the physical activity signal to define a second time period
25 associated with a second steady-state physical activity level of the subject, the second steady-state physical activity level of the subject corresponding to the same activity bin as the first steady-state physical activity level of the subject, including identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at the
30 second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level. The method further includes combining data from the other physiological signal also

obtained during the first and second time periods, and using the combined data from the other physiological signal to provide a resulting indicator.

Another example method includes detecting a plurality of activity levels using an accelerometer, determining for a candidate activity level an activity level bin value corresponding to a range of activity level values, and determining whether the candidate activity level was at steady state using bin values from activity levels detected before and after the candidate activity level. If the candidate activity level was at steady state, physiological data detected contemporaneously with the candidate activity level using an implantable medical device is added to one or more sum registers, and one or more counters is incremented. If the candidate activity level was not at steady state and a previous activity level was at steady state, the physiological data is averaged using the one or more sum registers and one or more counters. The method further includes aggregating the averaged physiological data with previous physiological data detected at an activity level corresponding to the same bin value, and storing aggregated physiological data averages.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a flow chart that illustrates an example method of monitoring physiological responses to steady state activity and providing a resulting indicator.

FIG. 2 is a flow chart that illustrates an example method of monitoring physiological responses to steady state activity, aggregating physiological data according to periods of steady state activity, and providing a resulting indicator.

FIGS. 3A and 3B are flow charts that illustrate an example method that includes analyzing a candidate activity level to identify steady state activity.

FIGS. 4A and 4B are flow charts that schematically illustrate an example method of monitoring physiological responses to steady state activity using activity bins.

FIGS. 5A and 5B are schematic illustrations of an example implantable device including circuits for detecting a physiological response to steady-state activity.

FIG. 6A is an example plot of heart and activity against time.

FIG. 6B is a table that illustrates example data that can be obtained using methods and apparatus for detecting a physiological response to steady-state activity.

5 FIG. 7A is an example graph that shows heart rate plotted against activity.

FIG. 7B is an example graph that shows heart rate plotted against activity for two instances in time.

FIG. 8 is an example graph that shows heart rate at 50 mG and heart rate slope ($dHR/dActivity$) plotted against days from baseline.

10 FIG. 9 is an example graph that shows stroke volume plotted against activity.

FIG. 10 is an example graph that shows stroke volume plotted against heart rate.

FIG. 11 is an example graph that shows time plotted against activity.

15 FIG. 12 is an example graph that shows tidal volume plotted against activity.

FIG. 13 is an example graph that shows respiration rate plotted against activity.

20 FIG. 14 is an example graph that shows respiratory rate plotted against tidal volume.

FIG. 15 is an example graph that shows pulmonary artery diastolic pressure plotted against activity.

FIG. 16 is an example graph that shows stroke volume plotted against pulmonary artery diastolic pressure.

25 FIG. 17 is an example graph that shows cardiac output plotted against activity.

FIG. 18 is an example graph that shows venous blood oxygen saturation plotted against activity.

30 FIG. 19 is an example graph that shows minute ventilation plotted against activity.

FIG. 20 is an example graph that shows minute ventilation plotted against cardiac output.

DETAILED DESCRIPTION

The following detailed description includes references to the accompanying drawings, which form a part of the detailed description. The drawings show, by way of illustration, specific embodiments in which the invention may be practiced. These embodiments are also referred to herein as “examples.” The following detailed description is not to be taken in a limiting sense, and the scope of the present invention is defined by the appended claims and their equivalents.

Physiological responses to periods of steady state activity are monitored using physiological sensors and processing circuitry. In an example, an implantable device includes one or more sensors that detect physiological parameters such as heart rate, tidal volume, respiratory rate, and/or total minute ventilation. The implantable device can also detect activity, for example using an accelerometer. In an example, the implantable device also includes a posture sensor. Periods of steady state activity are identified by monitoring activity data (e.g. accelerometer output) and deeming steady state to exist when the activity data meets certain criteria. In an example, a period of steady state activity is associated with a particular activity range, or “bin.” Steady state physiological data is stored and associated with a particular bin. In an example, physiological data is aggregated over a period of time (e.g. 24 hours) for multiple instances of activity in one or more activity ranges. In an example, steady state physiological data from different points in time (e.g. 30 days apart) is compared or otherwise processed to determine wellness and/or identify possible physiological conditions or changes.

FIG. 1, 2, 3A, 3B, 4A, and 4B are flow chart that illustrate example methods of monitoring physiological responses to steady state activity. FIGS. 5A and 5B are schematic illustrations of an example implantable device including circuits for detecting a physiological response to steady-state activity. FIG. 6A is a graph that shows heart beat and activity plotted against time. FIG. 6B is a table that illustrates example data that can be obtained using methods and apparatus for detecting physiological responses to steady-state activity. FIGS. 7A-20 are graphs that show relationships of detected physiological parameters and indicators that can be obtained from the relationships.

Referring now to the example method schematically illustrated in the flow chart of FIG. 1, at 105, a physical activity signal is detected from a human or animal subject using an implantable medical device. In an example, the physical activity signal is detected using an accelerometer, which is optionally
5 coupled to or contained within a device such as a pacer, defibrillator, neural stimulator, or other device. At 110, a different other physiological signal is detected from the subject using the implantable medical device. In an example, the different other physiological signal is detected using a sensor that senses, for example, an intrinsic electrical heart signal, heart sounds, thoracic impedance,
10 blood oxygen saturation, or intravascular blood pressure. In an example, the different other physiological signal includes heart rate, respiratory rate, stroke volume, tidal volume, venous blood oxygen saturation, cardiac output, or a blood pressure such as pulmonary artery diastolic pressure, systolic pressure, or mean pressure. At 115, the physical activity signal is processed to define a first
15 time period associated with a first steady-state physical activity level of the subject. In an example, the physical activity signal corresponds to a bin associated with a range of activity signal values. In an example, processing the physical activity signal includes identifying for the first time period a first beginning time at which the physical activity of the subject is deemed to be at
20 steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level. In an example, the physical activity of the subject is deemed to be at steady state when the detected activity has exhibited certain characteristics that are indicative of steady state for an amount of time. In an example, the physical activity of the
25 subject is deemed to be at steady state when the activity stays within a “bin range” of activity signal values for a specified period of time. In one example, the activity is deemed to be at steady state if the detected activity has been within a defined range (e.g. 10 milligrams (mG)) for a period of 20 seconds. In another example, the activity is deemed to be steady state if the detected activity has
30 been within a defined range (e.g. 20 mG) for a period of two minutes. In an example, two ranges are used – a first, smaller range (e.g. 10 mG) for a smaller period of time (e.g. one accelerometer reading or 20 seconds), and a second, larger range (e.g. 20 mG) for a larger period of time (e.g. two minutes). It is

understood that an accelerometer is not necessarily calibrated to mG, and could alternatively be calibrated to a different unit, or be uncalibrated, in which case ranges could be defined in raw detected values. In an example, the physical activity is deemed to have left the steady state when the difference between a particular activity bin value and a previous activity bin value or a sequence of activity bin values exceeds a defined value. In an example, the algorithm for determining whether a detected activity remains in steady state (or has left steady state) is the same as the algorithm for determining whether the activity has entered steady state.

10 FIG. 6A shows an example of heart rate (in beats per minutes (BPM)) and activity (in milli-G's) plotted against a time axis. The plot shows a lag between steady state detected activity and steady state physiological conditions (i.e. heart rate). In an example, for the purpose of using physiological data to provide a resulting indicator, physical activity is deemed to be at steady state after the detected physical activity has been in a specified range for a specified period of time. In an example, the specified period of time is about two or three minutes. For example, FIG. 6A shows a time period 610 from around minute 16 to minute 18, which is considered steady state physical activity. The graph shows steady state detected activity between about 30 mG and 40 mG during the time period 610. The time period 605 from around minute 13 to minute 16 also shows constant detected activity in this range. In an example, the three minute period 605 from minute 13 to minute 16 qualifies the following period 610 for consideration as steady state activity. This allows time for the heart rate to reach steady state after the detected activity level has reached a steady state. For example, the plot of heart rate against time shows that the heart rate moves to a steady state value of around 88 beats per minute during the period 610 from minute about 16 to minute 18. In contrast, during time period 605, the heart rate is not steady state, but moves from about 70 beats per minute to around 88 beats per minute. During period 615 from about minute 43 to 45, the detected activity is within a range of about 42 to 52 mG, but the period is too short for the heart beat to reach steady state, as can be seen from the graph.

Returning to FIG. 1, at 120, a first indicator is obtained by combining data from the other physiological signal (e.g. tidal volume) obtained during the

first period. In an example, the data is combined in an average (mean), a weighted average, a median, a range, or a standard deviation. In an example, obtaining the first indicator includes combining the data from the physiological signal obtained during the first period also with data from the physiological sensor obtained from a previous steady state period that falls into the same bin as the data obtained during the first period.

Referring again to FIG. 1, at 125, the physical activity signal is processed to define a second time period associated with a second steady-state physical activity level of the subject. It is understood that “first” and “second” are used herein to differentiate the time periods and do not refer to a sequential order. For example, the first period could come after the second period, or a third period could occur between the first and second period. In an example, the processing of the physical activity signal includes identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at a second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level. In an example, the second steady-state physical activity level corresponds to a different bin than the first steady-state activity level. In another example, the second steady-state physical activity level corresponds to the same bin as the first steady-state activity level, in which case the data from other physiological signal obtained during the first and second time periods is optionally combined. At 130, a second indicator is obtained by combining data from the other physiological signal obtained during the second time period. In an example, one or more additional other physiological signals are detected from the subject during periods of steady state activity, and one or more additional indicators are determined using the additional physiological indicators. In an example, respiratory rate, pulmonary artery diastolic pressure, and tidal volume are detected concurrently during steady state periods.

At 135, the first and second indicators are used to provide a resulting indicator. In an example, the resulting indicator is a value of a parameter (e.g. heart rate) at a particular activity level, or a characteristic (e.g. a slope, offset, difference, differential, or integral) of a relationship between two or more detected parameters, such as respiratory rate, tidal volume, and/or activity level,

for example. In an example, interpolation of data is also used to provide a resulting indicator. In an example, the resulting indicator is an indicator of a shift in a relationship between respiration rate and tidal volume. FIG. 10, for example, shows a shift in a relationship between stroke volume and heart rate.

5 FIG. 14 shows a shift in the relationship between respiration rate and tidal volume. In an example, an upward shift in the relationship between respiration rate and tidal volume is indicative of stiff lungs due to edema and/or heart failure decompensation.

In an example, if the first steady-state physical activity level and second

10 steady-state physical activity level correspond to the same bin, the first and second indicators are combined to produce a combined indicator, which is used to provide the resulting indicator. In an example, if the first steady-state physical activity level and second steady-state physical activity level correspond to different bins, the first and second indicators correspond to different activity

15 levels, as represented for example by points A and B in FIG. 7A.

FIG. 2 is a flow chart that illustrates an example method in which physiological data is aggregated by activity level. At 205, a physical activity signal is detected from a human or animal subject using an implantable medical device. In an example, the activity range of an accelerometer or other sensor is

20 divided into 20 activity bins. At 210, a different other physiological signal is contemporaneously detected from the subject using the implantable medical device. In an example, the different other physiological signal is detected using a sensor and is indicative of a parameter such as an intrinsic electrical heart signal, respiration, blood pressure, stroke volume, tidal volume, or venous blood

25 oxygen saturation. In an example, two or more different other physiological signals are detected. At 215, the physical activity signal is processed to define a first time period associated with a first steady-state physical activity level of the subject. Processing the physical activity signal includes identifying for the first time period a first beginning time at which the physical activity of the subject is

30 deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level. The first steady-state physical activity level corresponds to an activity bin. In an example, the processing includes comparing the activity bin

to a previous bin and/or sequence of bins to determine one or more differences and/or trends in activity levels or bins corresponding thereto.

At 220, the physical activity signal is processed to define a second time period associated with a second steady-state physical activity level of the subject. The processing includes identifying a second beginning time at which the physical activity of the subject is deemed to be at steady state at the second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level. The second steady-state physical activity level of the subject corresponds to the same activity bin as the first steady-state physical activity level of the subject.

At 225, data from the other physiological signal obtained during the first and second time periods is combined. In an example, the data is combined to determine aggregate average. A first average is determined for the first time period, a second average is determined for the second time period, and then the averages are combined to provide an aggregate average. In another example, a weighted averaged is determined, or the data from the first and second periods is combined and then averaged. At 230, the combined data from two or more activity levels is used to provide a resulting indicator, such as a slope or other differential, integral, difference, or other value that is indicative of a pathophysiological condition such as heart failure.

In an example, physiological signals such as respiratory rate and tidal volume are chronically monitored to monitor one or more physiological conditions. In an example, a second resulting indicator is obtained using data from a third and/or fourth steady state time period some time later (e.g. a week or more) than the first and second steady state time period. The resulting indicator obtained from the first and second time periods and the resulting indicator from the third and/or fourth time periods is used to monitor a physiological condition. In an example, a change in a relationship between respiratory rate and tidal volume is to monitor for stiff lungs due to edema or heart failure decompensation. For example, an upward shift in respiration vs. tidal volume during steady-state activity may be detected by monitoring physiological responses to steady state activity over the course of weeks, months, or years. FIG. 14 shows an upward shift in respiration v. tidal volume.

FIGS. 3A and 3B provide flow charts that illustrate additional example methods. At 305, a plurality of activity levels are detected using an accelerometer. In an example, an activity level is detected periodically by the accelerometer. In an example, an activity level is detected at least once every 10
5 seconds. At 310, an activity level bin value is determined for a candidate activity level. In an example, the candidate activity level is one of the detected activity levels. Alternatively, the candidate activity level is an average of one or more detected activity levels. The bins value corresponds to a range of activity levels. In an example, a bin value corresponds to a 10 mG range. For example,
10 a first bin corresponds to 0-10 mG, a second bin corresponds to 10 - 20 mG, etc. In an example, the bins overlap (e.g. 9 to 21, 19 to 31, 29 to 41, etc.) At 315, it is determined whether the candidate level is at steady state. In an example, activity levels detected before and after the candidate activity level are used to determine whether the candidate activity level occurred during a period of steady
15 state activity. FIGS. 4A and 4B show an example method of determining whether a candidate activity level is at steady state.

FIG. 3B illustrates an example method of determining whether the candidate activity level occurred during a period of steady state activity. At 355, it is determined whether the candidate activity level is within a first tolerance
20 range of one or more previous activity levels. In an example, it is determined whether the candidate activity level is within the first tolerance range of the immediately preceding activity level, i.e. the last data point before the candidate activity level. In an example, the first tolerance range is defined in terms of data values, e.g. 20 - 30 mG. Alternatively the range is a number of activity bins, e.g.
25 in the same bin, or within one bin. For example, if the range is one bin and the candidate activity level is in bin seven, the candidate activity level is deemed out of steady state if the bin value for the previous activity level is greater than eight or less than six. At 360, it is determined whether the candidate activity level is within a second tolerance range of a sequence of previous activity levels. In an
30 example, the second tolerance range is larger than the first tolerance range, and a greater variance in activity level is tolerated for the sequence of activity levels than for the previous activity level. In an example, the second tolerance range is 10-40 mG, or alternatively the second tolerance range is two bins. At 365, it is

determined whether activity levels are trending upward or trending downward, using activity levels detected before and after the candidate activity level. Trending analysis allows for identification of non-steady state periods where candidate activity levels fall within bin ranges but demonstrate rising or falling activity. Using activity levels detected both before and after the candidate activity level allows for better analysis of the candidate activity level in context than if only preceding activity levels were used.

Returning now to FIG. 3A, if the candidate activity level is at steady state, at 320 physiological data detected contemporaneously with the candidate activity level using an implantable medical device is added to a sum register. At 325, a counter is incremented. For example, if the candidate activity level is the ninth detected activity level in a period of steady state activity, the counter is incremented from eight to nine. As explained below, the counter is later used at 335 to determine an average, using the summed physiological data, when the period of steady state activity ends (e.g. $(\text{summed data})/(\text{counter value}) = \text{average}$). The method returns to 305 and additional activity levels are detected.

Returning to operation 315, if the candidate level is not at steady state, at 330, it is determined whether the candidate value represents the end of a period of steady state activity by determining whether one or more previous activity levels are at steady state. If the one or more previous activity levels were not at steady state, i.e. if the candidate value does not represent the end of a period of steady state activity, the method returns to 305. If the previous activity level was at steady state, at 335, an average is determined using the data in the sum register and the counter. In an example, the value in the sum register is divided by the counter value to determine the average physiological data value for the steady state period. At 340, the averaged physiological data is aggregated with previous physiological data detected at an activity level corresponding to the same bin value. Aggregated physiological data average is stored at 345, an aggregate counter is incremented at 350, and the process returns to 305. In an example, the aggregated physiological data is used to provide a resulting indicator. It is understood that the processing of the data does not necessarily occur as the data is collected. In an example, the data is collected first, and then

processed, in which case the method would return to 310 after 325, 330, and/or 345.

FIGS 4A and 4B are flowcharts that illustrate an example algorithm in more detail. The algorithm accumulates aggregated physiological data correlated to steady state activity. At 405, a value is read from an accelerometer. At 410, an average of a plurality of detected activity levels is determined. In an example, the average is a "BoxCar average." In an example, the box car average is an average of a number of sequential accelerometer values. In an example, accelerometer values are included in the BoxCar average for a number of averaging operations, and then purged from the BoxCar average. In an example, a BoxCar average determined at 410 includes seven values – three values preceding a candidate value and three values succeeding the candidate value (e.g. 14, 16, 19, XX, 18, 17, 18, wherein, XX is the candidate value.)

At 415, an activity level bin number (binNo) for a candidate accelerometer value is determined. The candidate value is a value for which a steady state analysis is conducted using a number of values taken before and after the candidate value. In an example, the candidate value is an average of a number of detected accelerometer values. A number of bins corresponding to ranges of activity levels are defined. In an example, bin 1 includes activity levels from 0-4 mG, bin 2 includes activity levels from 4-8 mG, bin 3 includes activity levels from 8-12 mG, etc. In an example, the activity level bin number for the candidate value is determined by dividing the candidate value by a bin width value (e.g. 4 mG) and truncating the quotient. For example, if the bin width value is 4, the binNo for activity levels 8, 9, 10, or 11 would be 2 and the binNo for activity levels 12, 13, 14, or 15 would be 3.

At 420, a steady state analysis is conducted. In an example, one or more algorithms are performed to determine whether the candidate value was taken during a period of steady state activity. FIG. 4B illustrates an example steady state method analysis method that uses the binNo for the candidate value and for values before and after the candidate value. At 470, the binNo for the candidate value is compared to the previous binNo value. If the binNo value is not within an acceptable range of the previous binNo value (e.g. 1 bin or 2 bins), it is concluded at 490 that the candidate value was not taken during a period of

steady state activity. If the binNo value is within an acceptable range of the previous binNo value, at 475, the binNo is compared to a plurality (e.g. six) preceding binNo values. If the binNo is not within an acceptable range of the preceding binNo values (e.g. 3 bins), it is concluded that the candidate value was not taken during a period of steady state activity. In an example, the acceptable range for the plurality of preceding binNo values is larger than the acceptable value for the previous binNo value. If the binNo value is within an acceptable range of the plurality of preceding binNo values, at 480 binNo values before and after the candidate binNo value are analyzed for trending. Alternatively, only values occurring before, or after, the candidate value are used in the trending analysis. If the binNo values do not exhibit trending, or if the binNo values exhibit trending below a threshold, it is concluded at 485 that the candidate value corresponds to a period of steady state activity. In the example illustrated in FIG. 4B, if one of the operations 470, 475 returns a No value, i.e. if the operation indicates that the candidate value was not taken during a period of steady state activity, the succeeding operations (e.g. operation 480) are not performed, thereby avoiding unnecessary processing and conserving processing power and/or battery energy. Alternatively, all three operations are performed regardless of the output of operation 475, 480. It is also understood that the operations 470, 475, 480 could be performed in a different order. For example, the trending analysis operation 480 could come first instead of last.

Returning to FIG. 4A, if the candidate value is determined to correspond to a period of steady state activity, at 425, a time counter is incremented. At 430, a buffer of previous binNo values is rotated. In an example, the buffer is a first in—first out (FIFO) buffer. The buffer of previous binNo values are used in operations 470, 475, and 480 in FIG. 4B. At 435, physiological data is added to sum registers. In an example, the physiological data includes one or more of heart rate (HR), tidal volume (TV), respiratory rate (RR), total minute ventilation (MV), pulmonary artery diastolic pressure (Ppa, dias), mixed venous blood oxygen saturation (Ven Sat), cardiac output (CardOut), and stroke volume of the heart (SV). It is understood that in alternative examples, some of the operations in FIG. 4A could be performed in a different order. For example, operations

425, 430, and 435, could occur in a different order or could occur simultaneously.

Referring again to FIG. 4A, if, at 420, the candidate value is determined to be during a non-steady state period, at 440, physiological data in the sum registers (if any) is processed (e.g. averaged) and added to physiological data arrays that aggregate data. In other words, the occurrence of a non-steady state value after a period of steady state activity triggers the aggregation of data in the sum registers into an aggregate data array. At 445, the FIFO buffer of binNo values before and after the current binNo value is rotated. At 450, the time counter is incremented.

FIGS. 5A is a schematic illustration of a medical device 500, lead 520, and electrodes 505, 510, 515 that are located at a location in a body, such as in, on or around a heart 501. The electrodes 505, 510, 515 are coupled to conductors that extend through the lead 520 and connect a header 530 on the medical device 500. Another electrode 525 is located on the medical device housing 535. In an example, the electrodes are used for antitachyarrhythmia therapy such as a defibrillation signal. In an example, electrodes 515, 525 or additional electrodes are used for sensing a physiological parameter, such as an intrinsic electrical heart signal.

FIG. 5B is a schematic illustration of an example configuration of the medical device 500 of FIG. 5A, electrodes, and sensors. The electrodes 505, 510, 515, 525 are coupled to a pulse generator 540 and optionally also to sensing circuitry 545, which are coupled to an analysis circuit 550. The analysis circuit 550 receives a signal from an activity sensor 555, which may be an accelerometer, for example, and at least one additional signal detected by one of the electrodes 505, 510, 515, 525 or another sensor, such as pressure sensor 560, or venous blood oxygen saturation sensor 565. In an example, a signal from a posture sensor 570 is also used in combination with the activity sensor 555 to detect periods of steady state activity.

FIG. 6B shows a table of example data values arranged according to steady state activity levels. These data would be obtained, for example, using the activity and physiological data maintained in the aggregate data array at 440 in FIG. 4A. The first column lists bin numbers (Bin No.) The second column

lists activity level ranges in milli-G's (thousandths of gravitational acceleration (3.81 m/s²). In the example table of FIG. 6B, the bin width is 25 mG. An accelerometer typically displays a value less than 25 when the patient is resting in a sitting, lying, or standing position. Accelerometer values of 25-50 typically correspond to walking slowly on a level surface, for example. Values higher than 50 correspond to faster walks, for example. Values in the 75-100 typically correspond to moderate exertion, such as light jogging. Accelerometer values greater than 100 typically refer to more strenuous exertion.

More or fewer bins could be used in other examples. In an example where more bins are used, each bin has a width of 5 mG. In another example, the bin width varies across the range of bins. In an example, a non-linear set of bins is used (e.g. 0 to 4 mG, 4 to 16 mG, 16 to 64 mG, 64 to 128 mG).

Referring again to FIGS. 6, columns three to eleven in the table provide data that relating to physiological responses to steady state activity for the various activity levels listed in the second column: The third column is the heart rate in beats per minute (BPM). The fourth column is the tidal volume (TV) in liters. The fifth column is the respiratory rate in breaths per minute (BPM). The sixth column is the minute ventilation in liters per min (L/min). The seventh column is the diastolic pressure of the pulmonary artery in millimeters of mercury (mm Hg). The eighth column is venous blood oxygen saturation. The ninth column is cardiac output in liters per minute (L/min). The tenth column is the stroke volume of the heart in milliliters (ml). The last column is the number of steady state minutes observed for each activity level bin.

Example methods and apparatus in accordance with this disclosure can provide some or all of the types of physiological data shown in FIG. 6B, depending on the specific embodiment and configuration. In an example, each cell of data in columns 3-9 of the table represents an average of a detected physiological parameter detected during one or more periods of steady state activity corresponding to the accelerometer range for that row. In an example, values for physiological variables are included in the reported average each time the activity sensor returns to a given bin range for a length of time that indicates steady state activity. In an example, data detected during a period of steady state activity is combined to provide a period average for the steady state period. If

the activity level returns to the steady state bin, an aggregate average, i.e. an average of the averages, is computed and provided in the table.

In an example, the total time spent at each level of activity is also tracked (see column 11 in FIG. 6B), which allows estimation of total exertion during the time period over which averaging continues. In an example, data is added to the table over a defined time period defined, such as 24 hours, 12 hours, or shorter periods, or over periods activated by the patient. In another example, data collection is initiated at the beginning of an exercise test. A typical exercise test lasts about 20 minutes. In an example, collection of data is initiated by the subject in whom the medical device is implanted.

In an example, data tables are stored or archived, and physiological data obtained at one time point is compared against data obtained at other time points.

Data gathered using the present methods and apparatus, such as the example shown in the table of FIG. 6B, is usable to monitor and/or diagnose one or more physiological conditions. FIGS. 7A to 17 are graphs that show examples of physiological data that are obtainable through examples of the presently described apparatus and methods. Example resulting indicators are obtainable from the graphs and/or data shown in FIGS. 7A-17. In some examples, graphing physiological data for a particular time point provides a useful resulting indicator. In FIG. 7A, for example, the slope of a heart rate vs. activity plot for a sample period (e.g. 24 hours) can be used as a resulting indicator. In other examples, a change in a resulting indicator is observable from data and/or graphs for multiple points in time, such as the shift of the two lines shown in FIG. 7B. Observed changes in physiological responses to steady state activity can indicate development or progression of a pathophysiological condition, such as heart failure. In another example, an indicator is monitored using a graph (or the underlying data) showing a parameter plotted against a time axis (e.g. FIG. 8).

In the graphs of FIGS. 7B and 9-17, data is provided for a Baseline time period, and for a later "Post" time period. While the present discussion focuses on physiological variables relating to the cardiac and/or respiratory systems, additional variables could be added or substituted to extend observations and

analysis to other organ systems, such as kidneys, leg muscles, or autonomic nervous system.

To understand the significance and utility of the information obtainable through the presently described algorithms and represented in FIG. 7A-17, it
5 may be useful to understand some principles of operation of the cardiovascular system. The heart and lungs together supply working muscles with the extra oxygen required by increasing activity. The amount of oxygen delivered to the tissues per minute is determined by the product of the heart rate, the stroke
10 volume of the heart, and the oxygen carrying capacity of the blood ($HR \times SV \times Ca, O_2$). As activity increases, controller mechanisms in the body cause increases in both heart rate and stroke volume. The amount of increase in each of these variables for a given increase in activity depends on multiple factors including health of the heart, fitness of the individual, and pharmacologic therapy. Diseased hearts have a reduced ability to increase stroke volume.
15 Because of this reduced ability to increase stroke volume, as the body tries to increase cardiac output required by a period of activity, the heart rate of a diseased heart for a given activity will be higher and/or rise more quickly than the heart rate for a healthy heart. Thus, a change in the rate of increase of either heart rate or stroke volume in response to activity is an indicator of a change in
20 either health and/or treatment status of the patient.

Referring now to FIG. 7A, a graph of heart rate against activity is shown. In a healthy person, heart rate typically increases linearly with external work intensity. Because activity as sensed by an accelerometer in implanted devices is related to external work intensity, the increase in heart rate plotted against
25 activity is typically linear. The heart rate increases because of stimuli originating from working muscles that tell the central nervous system of a need to increase oxygen delivery to working muscles. The rate of increase depends on the fitness level of the person (more fit individuals will have a smaller increase in heart rate than less fit people), disease condition of the heart, and
30 pharmacological therapy. A patient with diastolic heart disease will have reduced ability to increase stroke volume, and the heart rate at any given activity will tend to be higher. A person on beta blocker therapy will likely have a reduced heart rate for a given activity because the beta blocker drug acts directly

on the nerves endings in the heart that cause heart rate to increase during activity. The heart rate or rate of change of heart rate is usable, for example, as an indicator of fitness, the progression of disease, and/or the effectiveness of a therapy.

5 Referring now to FIG. 7B, two sets of data of shown on the graph, one for a "Baseline" measurement and one for a "Post" measurement. In an example, the Post measurement represents data collected after some time has elapsed from the "Baseline", or after some intervention such as change in medication. In an example, a curve-fitting operation is used to determine a curve
10 from the data. In FIG. 7B, a line has been determined for the baseline data and for the Post data. Interpolated values 705, 710 are also shown for each data set for an activity level of about 50 mG. In an example, a difference between heart rates at the 50 mG activity level for the Baseline and Post measurements is used as a resulting indicator. In an example, a difference between the interpolated
15 values is used as a resulting indicator. FIG. 7B shows a difference of 15 beats per minute at the interpolated values for 50 mG. In another example, an average difference over a range of values is used as a resulting indicator. In an example, the difference between the two lines is integrated over a range of activity levels and the integral is used as a resulting indicator. In another example, the slope of
20 one or both lines is used as an indicator. The slopes of the lines are shown numerically on FIG. 7B. In another example, the change in the slope (e.g. slope of Post line minus slope of Baseline line) is used as a resulting indicator.

FIG. 8 is a plot of heart rate at an activity level of 50 mG. FIG. 8 also shows periodic values for the first derivative (slope) of the heart rate against
25 activity, i.e. the slope of the heart rate data from the graph shown in FIG. 7B. In the example shown in FIG. 8, the heart rate and heart rate slope are plotted against Days from Baseline measurement, with two clinically significant events indicated. An increase in the heart rate slope and the HR @ 50 mG (e.g. around days 30-45) indicates that the patient's heart condition is deteriorating. After
30 treatment, both values dropped around day 45.

FIG. 9 is a plot of stroke volume vs. activity. The rate of increase (i.e. slope) of stroke volume with increasing activity is lower in the Post condition

than the baseline condition, indicating that heart condition has deteriorated since the baseline measurements.

FIG. 10 is a plot of stroke volume (in milliliters) against heart rate (in beats per minutes). The disease condition of the heart may be made more
5 evident by plotting heart rate and stroke volume together as shown in FIG. 9 rather than individually against activity. In an example, this plot amplifies a change in heart function compared with plots of either variable alone against activity. In an example, a reduction in SV at a heart rate of 100 beats per minute indicates a reduction in the heart's ability to pump blood. FIG. 10 shows
10 interpolated values for stroke volume at 100 beats per minute. The reduction in stroke volume in the "Post" condition compared to Baseline indicates a change in ability of the heart to pump blood.

FIG. 11 is a logarithmic plot that shows time spent at a given activity level. The higher time spent at zero activity during the Post measurement period
15 than the Baseline period suggests deteriorating heart condition. The reduced time spent at higher levels of activity during the Post period compared to the Baseline period also suggests deteriorating heart condition. An interpolated time value at an activity level of 50 mG is indicated. In an example, a difference
20 between interpolated values, or between a measured value and an interpolated value, is used as a resulting indicator. In the example shown, the interpolated value of time at 50 dropped by slightly over half, from 37 min to 18 minutes. Thus, time at 50 may be a particularly sensitive measure of patient well being.

FIGS. 12 shows tidal volume plotted against activity. FIG. 13 shows respiration rate plotted against activity. As activity increases, increasing HR and
25 SV to deliver more oxygen to the tissues, the lungs must bring in more fresh air to keep the incoming blood saturated with oxygen and to keep the blood at a normal level of Carbon Dioxide (CO₂) when the blood leaves the lungs. In a fashion similar to control of heart rate and stroke volume, the body increases respiratory rate (RR) and tidal volume (TV) as activity increases to control
30 oxygen saturation and CO₂ levels in arterial blood. The total ventilation is the product of respiration rate and tidal volume ($MV = RR \times TV$). The amount of increase in minute ventilation (MV) required by the body is dictated by the health of the lungs and by efficiency of the heart in delivering blood flow to the

lungs. It is known, for instance, that people with congestive heart failure need larger increase in MV for a given activity because the lungs become less efficient when cardiac output is reduced. In addition, stiff lungs affect the pattern of increasing respiration rate and tidal volume to reach a given target ventilation. When congestive heart failure becomes very severe, lungs become stiffer due to accumulated fluid in the interstitial spaces, resulting in a pattern of higher respiration and lower tidal volume compared to healthy lungs. Thus, tracking the pattern of change in respiration rate and tidal volume in response to steady state activity provides an indicator of the progression of congestive heart failure.

In an example, a change in minute ventilation during activity is tracked using a sensor that measures changes in electrical impedance across the lungs. With each tidal breath, impedance increases as the lung expands and decreases as they empty. Both relative tidal volume and respiration rate are obtainable from this signal. Relative tidal volume refers to a ratio of a present tidal volume to a baseline or maximum tidal volume. In another example, an actual quantified tidal volume is determinable from an external device that measures airflow directly (using a pneumotachograph) or measures chest wall dimensions.

Referring again to the graphs of tidal volume and respiration rate against activity shown in FIGS. 12 and 13, in the Post condition, for any given activity level, the tidal volume is higher than in the baseline condition, and the respiration rate is lower than in the baseline condition. This combination commonly occurs as lungs become mechanically stiffer due to accumulation of water caused by backup of fluid when diastolic pressure in the pulmonary artery increases in heart failure. In an example, one or both of these shifts is indicative of changing lung mechanics.

FIG. 14 shows respiratory rate (RR) plotted against Tidal Volume (TV). The upward shift in the curve in the "post" condition compared to Baseline indicates a change in lung mechanics. In an example, the upward shift indicates stiff lungs due to edema or heart failure decompensation. In an example, the graph of respiration rate against tidal volume amplifies changes in lung mechanics that are also detectable in the graphs of FIGS. 12 and 13.

FIG. 15 shows diastolic pressure in the pulmonary artery plotted against activity. FIG. 16 shows stroke volume plotted against pulmonary artery diastolic pressure. The heart cycle is split into two phases, an active contraction phase, called systole, and a passive filling phase, called diastole. During diastole, the heart fills with blood and during systole, the filled heart contracts to force the blood out into the arterial system. In diastole, blood flowing back to the heart enters the heart by largely passive means, and as the heart fills with blood the pressure inside rises. The amount of rise in pressure is one indication of heart health: a healthy heart can expand with little change in pressure, whereas a diseased heart is stiff and requires larger pressures to fill. In an example, a sensor detects diastolic pressure in the pulmonary artery, and the pressure needed to fill the heart is tracked along with stroke volume. A shift in the relationship between stroke volume and diastolic pressure in the pulmonary artery indicates a change in the stiffness of the heart.

Referring again to FIG. 15, pressure in the pulmonary artery measured at end of diastole ($P_{pa, dias}$) is plotted against activity for Baseline and Post conditions. The increased pressure at all activities in the Post measurements indicates a change in cardiac mechanics or fluid status. In an example, an increase in pulmonary artery diastolic pressure indicates fluid retention and heart failure decompensation. In another example, an upward shift in slope indicates a change in stiffness of the heart.

FIG. 16 shows stroke volume plotted against diastolic pressure in the pulmonary artery for baseline and post conditions. A drop in the stroke volume for all pulmonary artery diastolic pressure values indicates reduced compliance (increased stiffness) of the heart. A reduction in the slope of the lines also indicates reduced compliance of the heart. In an example, the graph and data shown in FIG. 16 is used to track changes in heart condition. In another example, the graph and/or data shown in FIG. 16 is used to diagnose a heart conditions. A rise in pulmonary artery diastolic pressure does not necessarily indicate a stiff heart. For example, pulmonary artery diastolic pressure will also rise if arterial pressure is too high (systemic hypertension) for the left ventricle to completely empty during systole. A healthy heart pumping against arterial hypertension would likely show higher SV in the graphs of FIGS. 15 and 16.

FIG. 17 shows cardiac output plotted against activity. Cardiac output is the product of stroke volume and heart rate ($\text{CardOut} = \text{SV} \times \text{HR}$). In normal individuals, this relationship is typically constant, and does not vary with conditioning level of the subject. In an example, a change in the CardOut vs. activity relationship (e.g. a downward offset of the line in FIG. 17) is used as an indicator of heart disease. In another example, a reduction of the slope of CardOut vs. activity relationship indicates progression of heart disease. In an example, one or more sensors measures stroke volume or cardiac output.

In another example, venous oxygen saturation level of blood is used as an indicator of cardiac status. FIG. 18 is a graph that shows venous oxygen saturation (VenSat) plotted against activity for Baseline and Post timeframes. The reduction in VenSat at activities above the resting level at the Post time indicates an inability of the heart to increase Cardiac Output to support tissue oxygen demands. As the heart increases its output with activity, increased blood flow goes to working muscles, which extract oxygen to support increased metabolism. The amount of extraction is determined by a mass balance relationship called the Fick Equation, $\text{VO}_2 = \text{CardOut} \times (\text{CaO}_2 - \text{CvO}_2)$, where VO_2 is oxygen consumption, CardOut is the cardiac output and $\text{CaO}_2 - \text{CvO}_2$ is the difference in oxygen content of arterial and mixed venous blood, respectively. Re-arranging the Fick equation shows that this difference reflects the balance between VO_2 and CardOut: $(\text{CaO}_2 - \text{CvO}_2) = \text{VO}_2 / \text{CardOut}$. If CardOut is low compared to VO_2 , the $\text{CaO}_2 - \text{CvO}_2$ difference must be larger, as the working muscles need to extract more oxygen per unit of blood when blood flow is inadequate. Because the CaO_2 is relatively constant, the $\text{CaO}_2 - \text{CvO}_2$ difference can only widen by reducing CvO_2 . The content of oxygen in the blood is the product of the degree of O_2 saturation of the Hemoglobin molecule, VenSat, times blood content of hemoglobin. Because blood content of hemoglobin also stays constant, variations in VenSat will reflect the balance of VO_2 and CardOut. Conditions in which CardOut is insufficient will cause VenSat to drop, as illustrated in FIG. 18. A change in the venous blood oxygen saturation at a steady state activity level is usable as an indicator of heart condition. In an example, a reduced venous blood oxygen saturation at a given

activity level indicates a reduced ability of the heart to supply oxygen to tissues and a progression of heart disease.

FIG. 19 is a graph that shows minute ventilation plotted against activity. In an example, an increase in the slope of minute ventilation vs. activity or an
5 increase in minute ventilation at a particular activity level indicates abnormal lung function, such edema.

FIG. 20 is a graph that shows minute ventilation plotted against cardiac output. In an example, increasing minute ventilation for a given cardiac output indicate deteriorating heart condition.

10 The above specification, examples and data provide a complete description of the manufacture and use of the composition of the invention. Since many embodiments of the invention can be made without departing from the scope of the invention, the invention resides in the claims hereinafter
appended.

15

WHAT IS CLAIMED IS:

1. A system comprising:
 - an implantable activity sensor, configured for detecting a physical activity
 - 5 signal from a human or animal subject;
 - an implantable first other physiological sensor, configured for detecting a first other physiological signal from the subject, the first other physiological signal being different from the physical activity signal;
 - a signal processor, configured to process the physical activity signal to define a
 - 10 first time period associated with a first steady-state physical activity level of the subject, including identifying for the first time period a first beginning time at which the physical activity of the subject is deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level, the signal processor obtaining a first indicator by
 - 15 using data from the first other physiological signal obtained during the first time period, the signal processor processing the physical activity signal to define a second time period associated with a second steady-state physical activity level of the subject, including identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at the second steady-
 - 20 state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level, the signal processor obtaining a second indicator by using data from the first other physiological signal obtained during the second time period, the signal processor using the first and second indicators to provide a first resulting indicator.
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2. The system of claim 1, wherein the processor includes a first activity bin for a range of activity levels comprising the first steady state physical activity level.

3. The system of claim 2, in which the processor includes a second activity bin for a range of activity levels comprising the second steady-state physical activity level, wherein the first and second activity bins correspond to different physical activity levels.
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4. The system of claim 2, in which the second steady-state physical activity level corresponds to the same first activity bin as the first steady-state physical activity level.
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5. The system of claim 4, wherein the second time period occurs after the first time period, and the second indicator combines data from the first other physiological signal obtained during the second time period with data from the first other physiological signal obtained during the first time period.
- 15
6. The system of claim 5, wherein the processor is configured to process the physical activity signal to define a third time period associated with a third steady-state physical activity level of the subject, including identifying for the third time period a third beginning time at which the physical activity of the subject is deemed to be at steady-state at the third steady-state physical activity level, and a third ending
- 20
- time at which the subject leaves the third steady-state physical activity level, the third time period occurring between the first time period and the second time period, and obtaining a third indicator by combining data from the first other physiological signal obtained during the third time period.
- 25
7. The system of claim 1, further comprising an implantable second other physiological signal sensor, configured for detecting a second other physiological signal from the subject, and obtaining third and fourth indicators by using data from the second other physiological signal obtained during the respective first and second time periods, wherein using the first and second indicators to provide the resulting

indicator includes using the first, second, third, and fourth indicators to provide the resulting indicator.

8. The system of claim 1, wherein the processor is configured for obtaining the
5 first indicator by using data from the first other physiological signal obtained during the first time period by averaging the data from the first other physiological signal obtained during the first time period.

9. The system of claim 1, wherein the resulting indicator includes an offset, a
10 difference, a derivative, an interpolation, or an integral.

10. The system of claim 1, wherein the resulting indicator provides information about a relationship between heart rate and activity.

11. The system of claim 1, wherein the resulting indicator provides information
15 about a relationship between stroke volume and activity or heart rate.

12. The system of claim 1, wherein the resulting indicator provides information
20 about a relationship between at least two of respiratory rate, activity, and tidal volume.

13. The system of claim 1, wherein the resulting indicator provides information about a relationship between an intravascular pressure or venous blood oxygen saturation and activity level or one or more other physiological parameters.

14. A system comprising:
25 an implantable activity sensor, configured for detecting a physical activity signal from a human or animal subject, the physical activity signal falling within an activity range divided into activity bins;

an implantable first other physiological sensor, configured for contemporaneously detecting a different first other physiological signal, from the subject;

a processor, configured for processing the physical activity signal to define a first time period associated with a first steady-state physical activity level of the subject, including identifying for the first time period a first beginning time at which the physical activity of the subject is deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level, the first steady-state physical activity level corresponding to an activity bin, the processor configured for processing the physical activity signal to define a second time period associated with a second steady-state physical activity level of the subject, the second steady-state physical activity level of the subject corresponding to the same activity bin as the first steady-state physical activity level of the subject, including identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at the second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state physical activity level, and the processor combining data from the first other physiological signal also obtained during the first and second time periods, and the processor determining a resulting indicator using the combined data from the first other physiological signal.

15. The system of claim 14, in which the processor is configured for processing the physical activity signal to define a third time period associated with a third steady-state physical activity level of the subject, including identifying for the third time period a third beginning time at which the physical activity of the subject is deemed to be at steady state at the third steady-state physical activity level, and a third ending time at which the subject leaves the third steady-state physical activity level, the third steady-state physical activity level corresponding to an activity bin, and wherein the processor is configured for processing the physical activity signal to define a fourth time period associated with a fourth steady-state physical activity level of the subject,

the fourth steady-state physical activity level of the subject corresponding to the same activity bin as the first steady-state physical activity level of the subject, including identifying for the fourth time period a fourth beginning time at which the physical activity of the subject is deemed to be at steady state at the fourth steady-state physical activity level, and a fourth ending time at which the subject leaves the fourth steady-state physical activity level, and wherein the processor is configured for combining data from the other physiological signal also obtained during the third and fourth time periods, and wherein the processor determines a second resulting indicator by using the combined data from the first other physiological signal obtained during the third and fourth time periods, and wherein the processor is configured for using the first and second resulting indicators to monitor a physiological condition of the subject.

16. The system of claim 14, wherein the processor is configured for combining data from the first other physiological signal obtained during the first and second time periods by determining a first average of data obtained during the first time period, obtaining a second average of data obtained during the second time period, and combining the first average and the second average.

17. The system of claim 14, wherein the processor is configured for determining the first resulting indicator using the combined data from the first other physiological signal by determining a heart rate, stroke volume, tidal volume, or respiration rate for a steady state activity level.

18. The system of claim 14, wherein the processor is configured for determining the first resulting indicator using the combined data from the first other physiological signal by determining a venous blood oxygen saturation or pulmonary artery diastolic pressure for a steady state activity level.

19. A system comprising:
an implantable accelerometer, configured for detecting a plurality of activity levels;
a processor, including activity level bin counters and sum registers, the
5 processor configured for determining for a candidate activity level an activity level bin value corresponding to a range of activity level values, and for determining whether the candidate activity level was at steady state using bin values from activity levels detected before and after the candidate activity level and, when the candidate activity level is determined to be at steady state, then adding to one or more of the sum
10 registers physiological data detected contemporaneously with the candidate activity level, and incrementing one or more of the counters, and when the activity level is determined to be not at steady state and a previous activity level was at steady state, then averaging the physiological data using the one or more sum registers and one or more of the counters, and wherein the processor is further configured for aggregating
15 the averaged physiological data with previous physiological data detected at an activity level corresponding to the same bin value, and wherein the processor includes or is coupled to a memory for storing aggregated physiological data averages.

20. The system of claim 19, wherein the processor is configured for determining
20 whether the candidate activity level was at steady state by determining whether the candidate activity level is within a first range of a previous activity level, determining whether the candidate activity level is within a second range of a sequence of previous activity levels, the second range larger than the first range, and determining whether activity levels are trending upward or downward using activity levels detected before
25 and after the candidate activity level.

21. The system of claim 19, wherein the processor is configured for determining
whether the candidate activity level was at steady state by determining whether the bin
value for the candidate activity level is within a first range of a bin value for a
30 previous activity level, determining whether the bin value for the candidate activity

level is within a second range of bin values for a sequence of previous activity levels, the second range larger than the first range, and determining whether activity levels are trending upward or downward using bin values from activity levels detected before and after the candidate activity level.

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22. The system of claim 21, wherein the first range is one bin and the second range is two bins.

23. The system of claim 19, further comprising a resulting indicator determined by using the aggregated physiological data averages.

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24. The system of claim 23, wherein the resulting indicator is determined using the aggregated physiological data averages to aggregate heart rate, stroke volume, tidal volume, respiratory rate, pulmonary artery diastolic pressure data, or venous blood oxygen level.

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25. The system of claim 19, wherein the processor is configured for determining whether the candidate activity level was at steady state using bin values from activity levels detected before and after the candidate activity level by deeming the candidate activity level as not at steady state if activity levels from a specified amount of time preceding the candidate activity level are not within a specified range.

20

26. A machine-assisted method comprising:
detecting a physical activity signal, using an implantable medical device, from a human or animal subject;
detecting a different first other physiological signal, from the subject, using the implantable medical device;
processing the physical activity signal to define a first time period associated with a first steady-state physical activity level of the subject, including identifying for the first time period a first beginning time at which the physical activity of the subject

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is deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level;

obtaining a first indicator by combining data from the first other physiological
5 signal obtained during the first time period;

processing the physical activity signal to define a second time period
associated with a second steady-state physical activity level of the subject, including
identifying for the second time period a second beginning time at which the physical
activity of the subject is deemed to be at steady state at the second steady-state
10 physical activity level, and a second ending time at which the subject leaves the
second steady-state physical activity level;

obtaining a second indicator by combining data from the first other
physiological signal obtained during the second time period; and

using the first and second indicators to provide a resulting indicator.
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27. The method of claim 26, wherein the first steady state physical activity level corresponds to a bin associated with a range of activity levels.

28. The method of claim 27, in which the second steady-state physical activity
20 level corresponds to a different activity bin than the first steady-state physical activity
level.

29. The method of claim 27, in which the second steady-state physical activity
level corresponds to the same activity bin as the first steady-state physical activity
25 level.

30. The method of claim 29, wherein the second time period occurs after the first
time period, and the obtaining a second indicator by combining data from the first
other physiological signal obtained during the second time period includes combining

data from the first other physiological signal obtained during the second time period with data from the first other physiological signal obtained during the first time period.

31. The method of claim 30, further comprising processing the physical activity
5 signal to define a third time period associated with a third steady-state physical
activity level of the subject, including identifying for the third time period a third
beginning time at which the physical activity of the subject is deemed to be at steady
state at the third steady-state physical activity level, and a third ending time at which
the subject leaves the third steady-state physical activity level, the third time period
10 occurring between the first time period and the second time period; and
obtaining a third indicator by combining data from the first other physiological
signal obtained during the third time period.

32. The method of claim 26, further comprising detecting a second other
15 physiological signal, from the subject, using the implantable medical device, and
obtaining third and fourth indicators by combining data from the second other
physiological signal obtained during the respective first and second time periods,
wherein using the first and second indicators to provide a resulting indicator includes
using the first, second, third and fourth indicators.

20
33. The method of claim 26, wherein obtaining a first indicator by combining data
from the first other physiological signal obtained during the first time period includes
averaging the data from the first other physiological signal obtained during the first
time period.

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34. The method of claim 26, wherein the resulting indicator includes an offset, a
difference, a derivative, an interpolation, or an integral.

35. The method of claim 26, wherein the resulting indicator provides information
30 about a relationship between heart rate and activity.

36. The method of claim 26, wherein the resulting indicator provides information about a relationship between stroke volume and activity or heart rate.

37. The method of claim 26, wherein the resulting indicator provides information
5 about a relationship between at least two of respiratory rate, activity, and tidal volume.

38. The method of claim 26, wherein the resulting indicator provides information about a relationship between an intravascular pressure or venous blood oxygen saturation and activity level or one or more other physiological parameters.

10

39. A machine-assisted method comprising:

detecting a physical activity signal, using an implantable medical device, from a human or animal subject, the physical activity signal falling within an activity range divided into activity bins;

15

contemporaneously detecting a different first other physiological signal, from the subject, using the implantable medical device;

20

processing the physical activity signal to define a first time period associated with a first steady-state physical activity level of the subject, including identifying for the first time period a first beginning time at which the physical activity of the subject is deemed to be at steady state at the first steady-state physical activity level, and a first ending time at which the subject leaves the first steady-state physical activity level, the first steady-state physical activity level corresponding to an activity bin;

25

processing the physical activity signal to define a second time period associated with a second steady-state physical activity level of the subject, the second steady-state physical activity level of the subject corresponding to the same activity bin as the first steady-state physical activity level of the subject, including identifying for the second time period a second beginning time at which the physical activity of the subject is deemed to be at steady state at the second steady-state physical activity level, and a second ending time at which the subject leaves the second steady-state

30

physical activity level;

combining data from the first other physiological signal also obtained during the first and second time periods; and

using the combined data from the first other physiological signal to provide a resulting indicator.

5

40. The method of claim 39, further comprising:

processing the physical activity signal to define a third time period associated with a third steady-state physical activity level of the subject, including identifying for the third time period a third beginning time at which the physical activity of the subject is deemed to be at steady state at the third steady-state physical activity level, and a third ending time at which the subject leaves the third steady-state physical activity level, the third steady-state physical activity level corresponding to an activity bin;

15 processing the physical activity signal to define a fourth time period associated with a fourth steady-state physical activity level of the subject, the fourth steady-state physical activity level of the subject corresponding to the same activity bin as the first steady-state physical activity level of the subject, including identifying for the fourth time period a fourth beginning time at which the physical activity of the subject is deemed to be at steady state at the fourth steady-state physical activity level, and a fourth ending time at which the subject leaves the fourth steady-state physical activity level;

20 combining data from the first other physiological signal also obtained during the third and fourth time periods;

25 using the combined data from the first other physiological signal obtained during the third and fourth time periods to provide a second resulting indicator; and

using the resulting indicator from the first and second time periods and the resulting indicator from the third and fourth time periods to monitor a physiological condition of the subject.

41. The method of claim 39, wherein combining data from the first other physiological signal also obtained during the first and second time periods includes determining a first average of data obtained during the first time period, obtaining a second average of data obtained during the second time period, and combining the first average and the second average.

42. The method of claim 39, wherein using the combined data from the first other physiological signal to provide a resulting indicator includes determining a heart rate, stroke volume, tidal volume, or respiration rate for a steady state activity level.

43. The method of claim 39, wherein using the combined data from the first other physiological signal to provide a resulting indicator includes determining a venous blood oxygen saturation or pulmonary artery diastolic pressure for a steady state activity level.

44. A method comprising:
detecting a plurality of activity levels using an accelerometer;
determining for a candidate activity level an activity level bin value corresponding to a range of activity level values;
determining whether the candidate activity level was at steady state using bin values from activity levels detected before and after the candidate activity level;
if the candidate activity level was at steady state, adding to one or more sum registers physiological data detected contemporaneously with the candidate activity level using an implantable medical device, and incrementing one or more counters;
if the candidate activity level was not at steady state and a previous activity level was at steady state:
averaging the physiological data using the one or more sum registers and one or more counters;
aggregating the averaged physiological data with previous physiological data detected at an activity level corresponding to the same bin value; and

storing aggregated physiological data averages.

45. The method of claim 44, wherein determining whether the candidate activity level was at steady state includes:

- 5 determining whether the candidate activity level is within a first range of a previous activity level;
- determining whether the candidate activity level is within a second range of a sequence of previous activity levels, the second range larger than the first range; and
- determining whether activity levels are trending upward or downward using
- 10 activity levels detected before and after the candidate activity level.

46. The method of claim 44, wherein determining whether the candidate activity level was at steady state includes:

- determining whether the bin value for the candidate activity level is within a
- 15 first range of a bin value for a previous activity level;
- determining whether the bin value for the candidate activity level is within a second range of bin values for a sequence of previous activity levels, the second range larger than the first range; and
- determining whether activity levels are trending upward or downward using
- 20 bin values from activity levels detected before and after the candidate activity level.

47. The method of claim 46, wherein the first range is one bin and the second range is two bins.

- 25 48. The method of claim 44, further comprising using the aggregated physiological data averages to provide a resulting indicator.

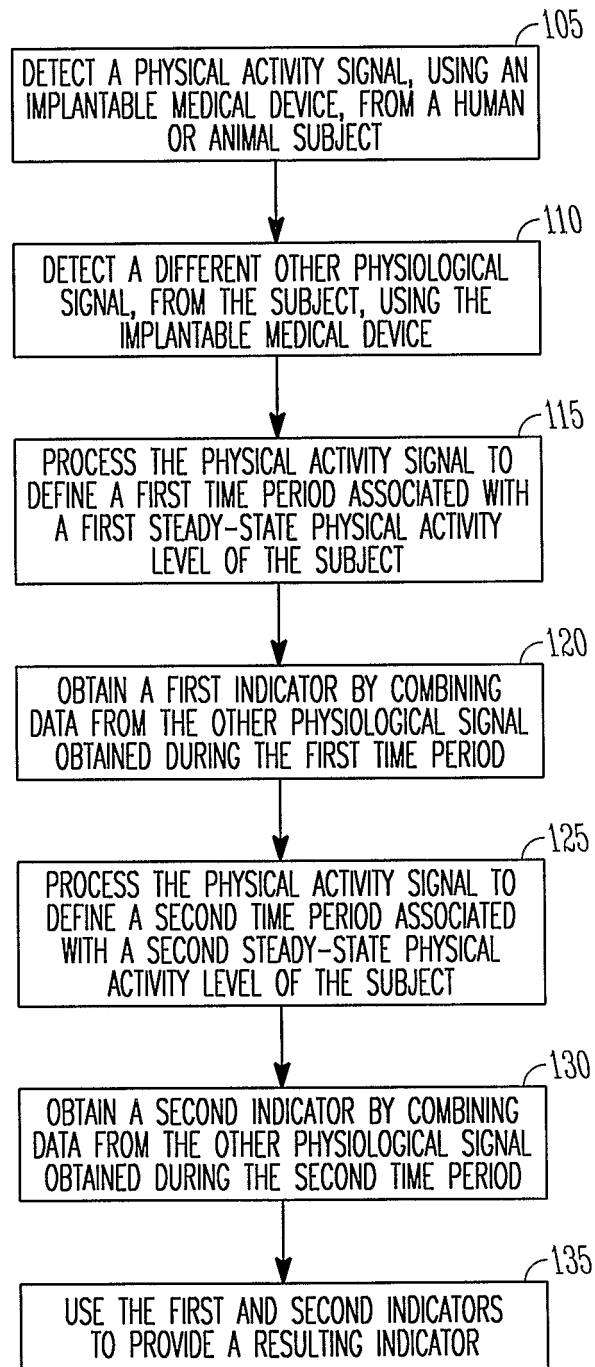
49. The method of claim 48, wherein using the aggregated physiological data averages to provide a resulting indicator includes aggregating heart rate, stroke volume, tidal volume, respiratory rate, pulmonary artery diastolic pressure data, or venous blood oxygen level.

5

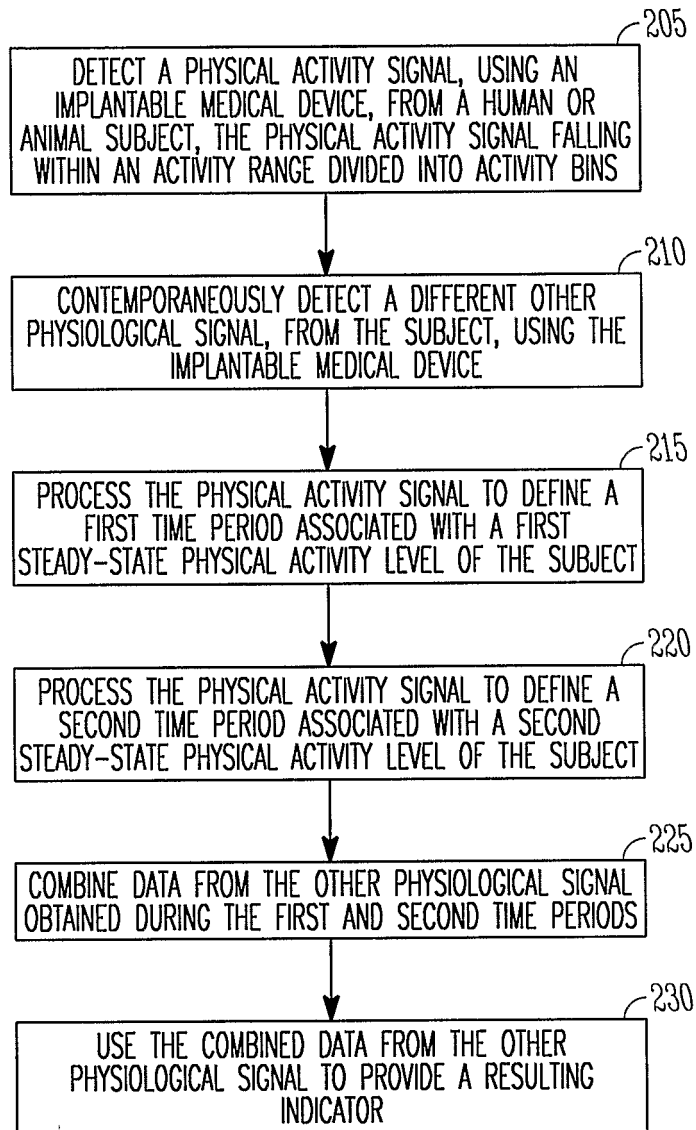
50. The method of claim 44, wherein determining whether the candidate activity level was at steady state using bin values from activity levels detected before and after the candidate activity level includes deeming the candidate activity level as not at steady state if activity levels from a specified amount of time preceding the candidate

10 activity level are not within a specified range.

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*FIG. 1*

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*FIG. 2*

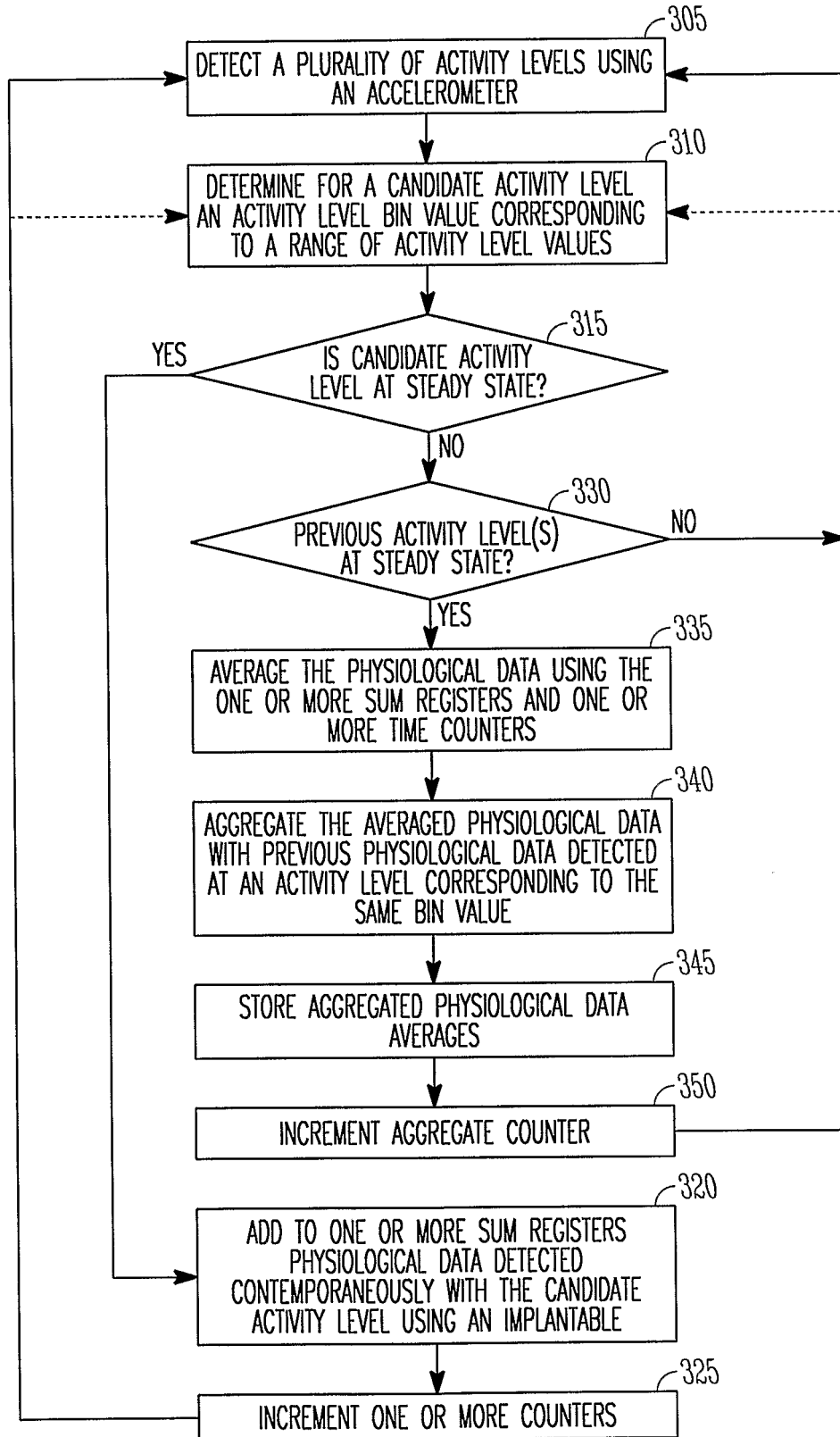
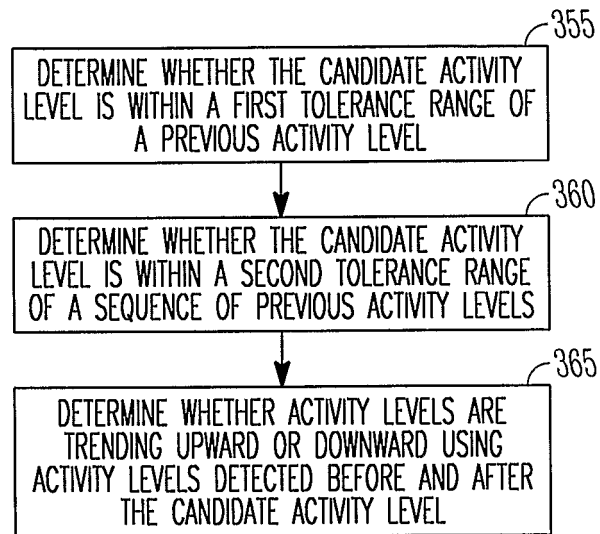


FIG. 3A

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*FIG. 3B*

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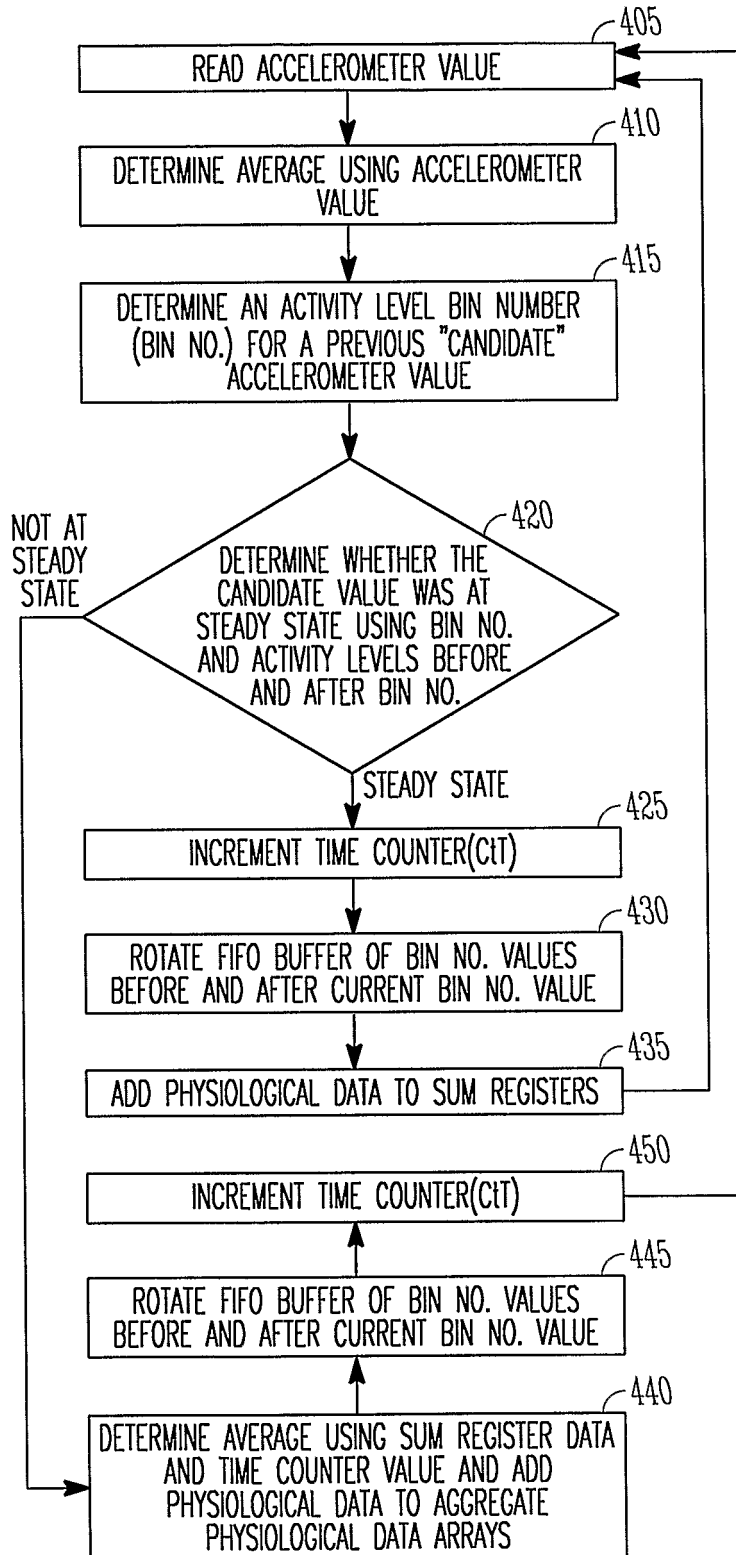


FIG. 4A

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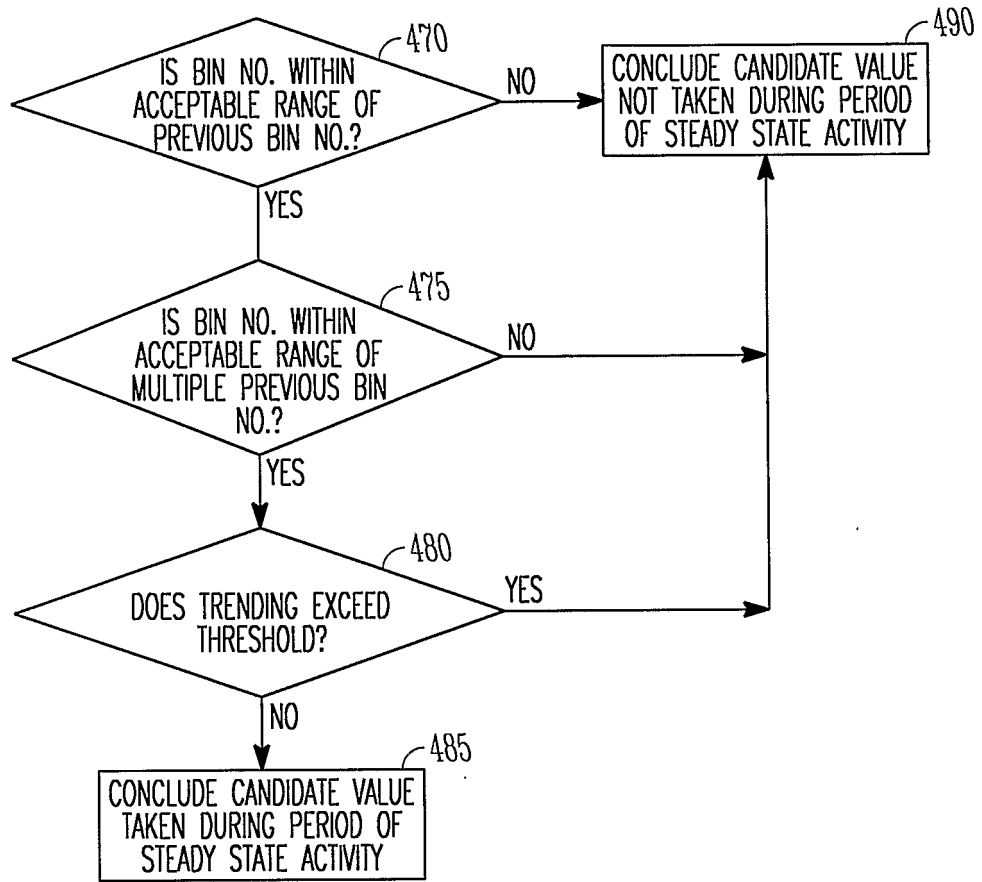


FIG. 4B

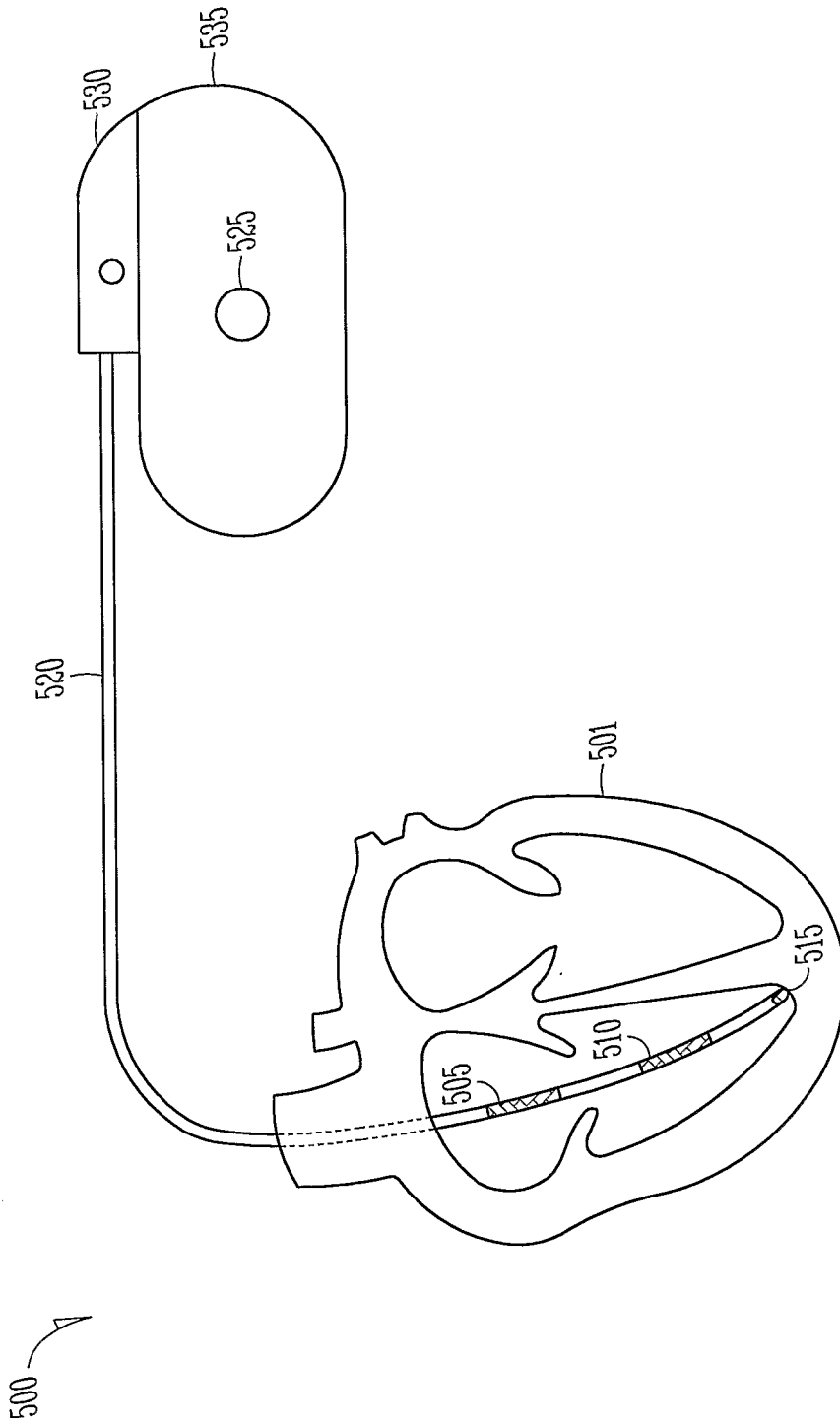


FIG. 5A

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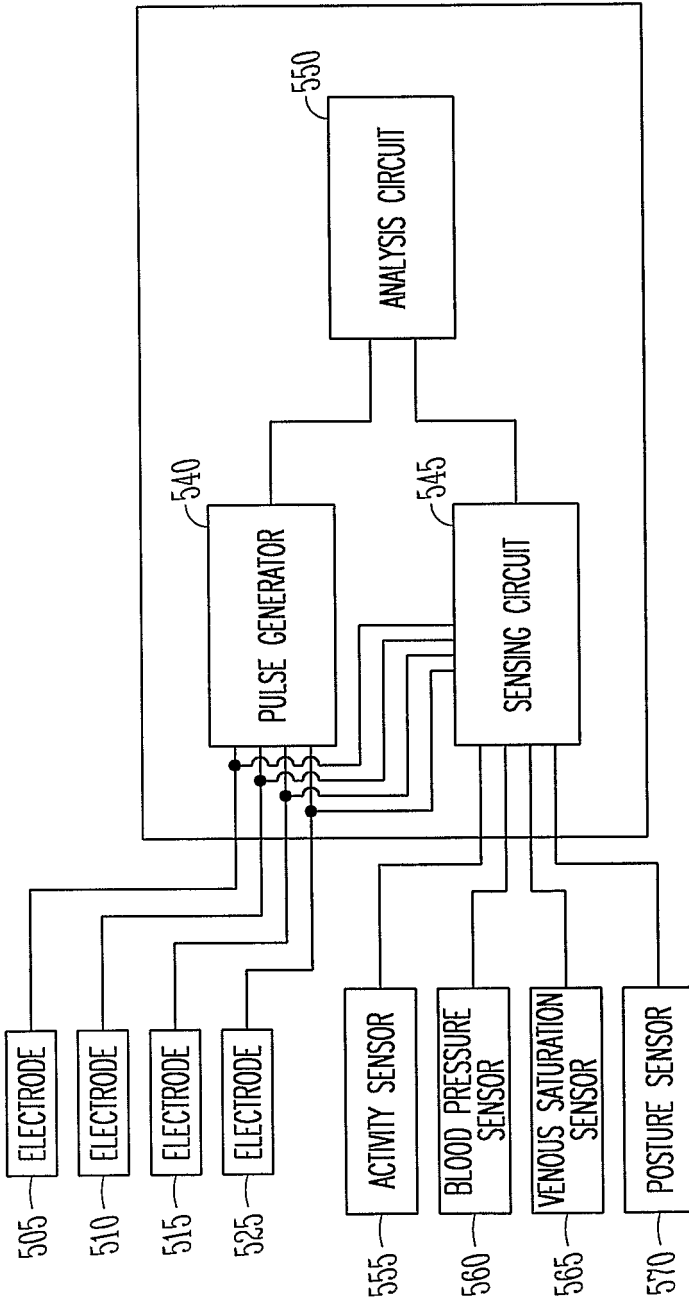


FIG. 5B

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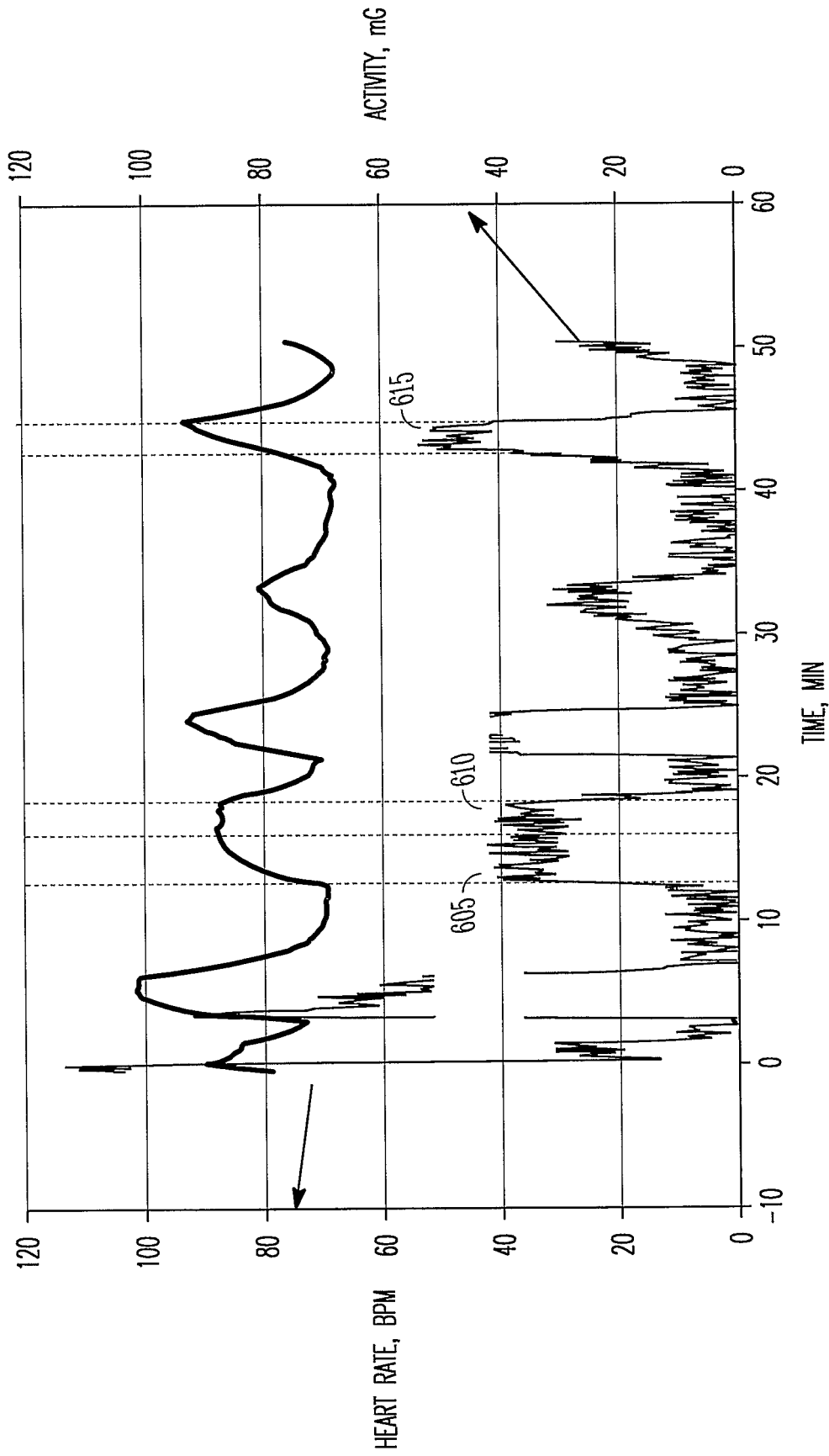


FIG. 6A

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PHYSIOLOGICAL RESPONSE TO ACTIVITY TABLE										
BIN NO.	ACTIVITY RANGE (mG)	PHYSIOLOGICAL RESPONSES								
		HR BPM	TV LITER	RR BPM	MV L/min.	Ppa,DIAS mmHg	VEN SAT %	CARDOUT L/min.	SV ml	MIN
1	0-10	65	0.80	10	8.0	12	59.2%	4.0	62	378
2	10-20	86	1.20	12	14.4	13	45.7%	5.6	65	154
3	20-30	91	1.45	13	18.85	14	42.1%	5.9	65	99
4	30-40	98	1.60	14	22.4	15	37.7%	6.3	65	42
5	40-50	103	1.75	15	26.25	16	33.9%	6.8	66	29
6	50-60	110	1.90	17	32.3	17	28.7%	7.4	67	18
7	60-70	117	2.0	19	38	19	24.4%	8.1	69	14
8	70-80	125	2.15	21	45.2	20	20.9%	8.7	70	8
9	80-90	131	2.2	24	57.6	21	19.1%	9.0	69	5
10	90-100	140	2.25	26	58.5	22	16.9%	9.5	68	3
11	100-110	149	2.24	27	60.48	23	15.8%	10.0	67	1

LEGEND

HR BPM:	HEART RATE IN BEATS PER MINUTE
TV LITER:	TIDAL VOLUME IN LITERS
RR BPM:	RESPIRATION RATE IN BEATS PER MINUTE
MV L/min:	MINUTE VENTILATION IN LITERS PER MINUTE
Ppa, DIAS mmHG:	PULMONARY ARTERY DIASTOLIC PRESSURE IN MILLIMETERS OF MERCURY
VEN SAT%:	OXYGEN SATURATION OF BLOOD IN VEINS, IN PERCENTAGE TERMS
CARDOUT L/min:	CARDIAC OUTPUT IN LITERS PER MINUTE
SV ml:	STROKE VOLUME IN MILLILITERS
MIN:	MINUTES OF ACTIVITY

FIG. 6B

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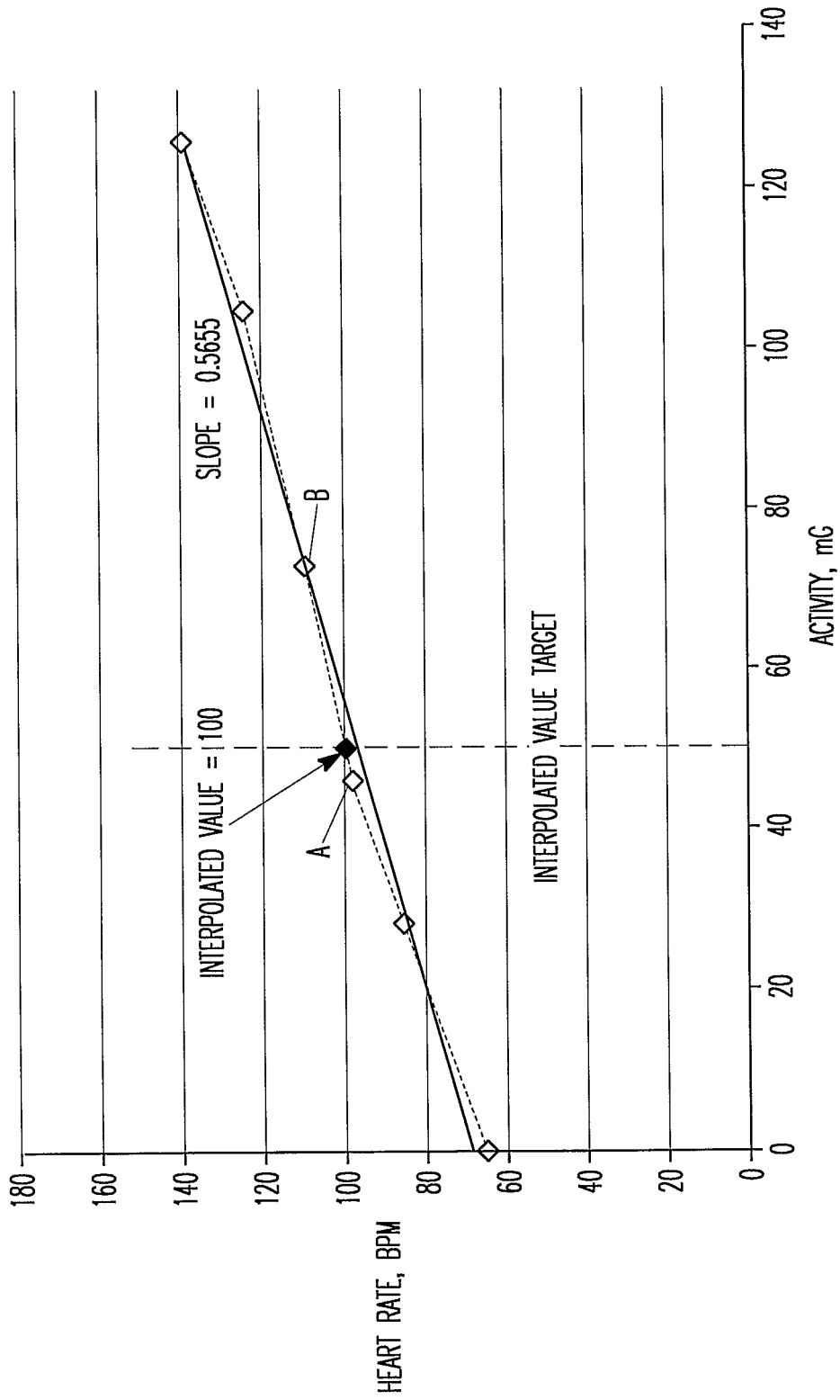


FIG. 7A

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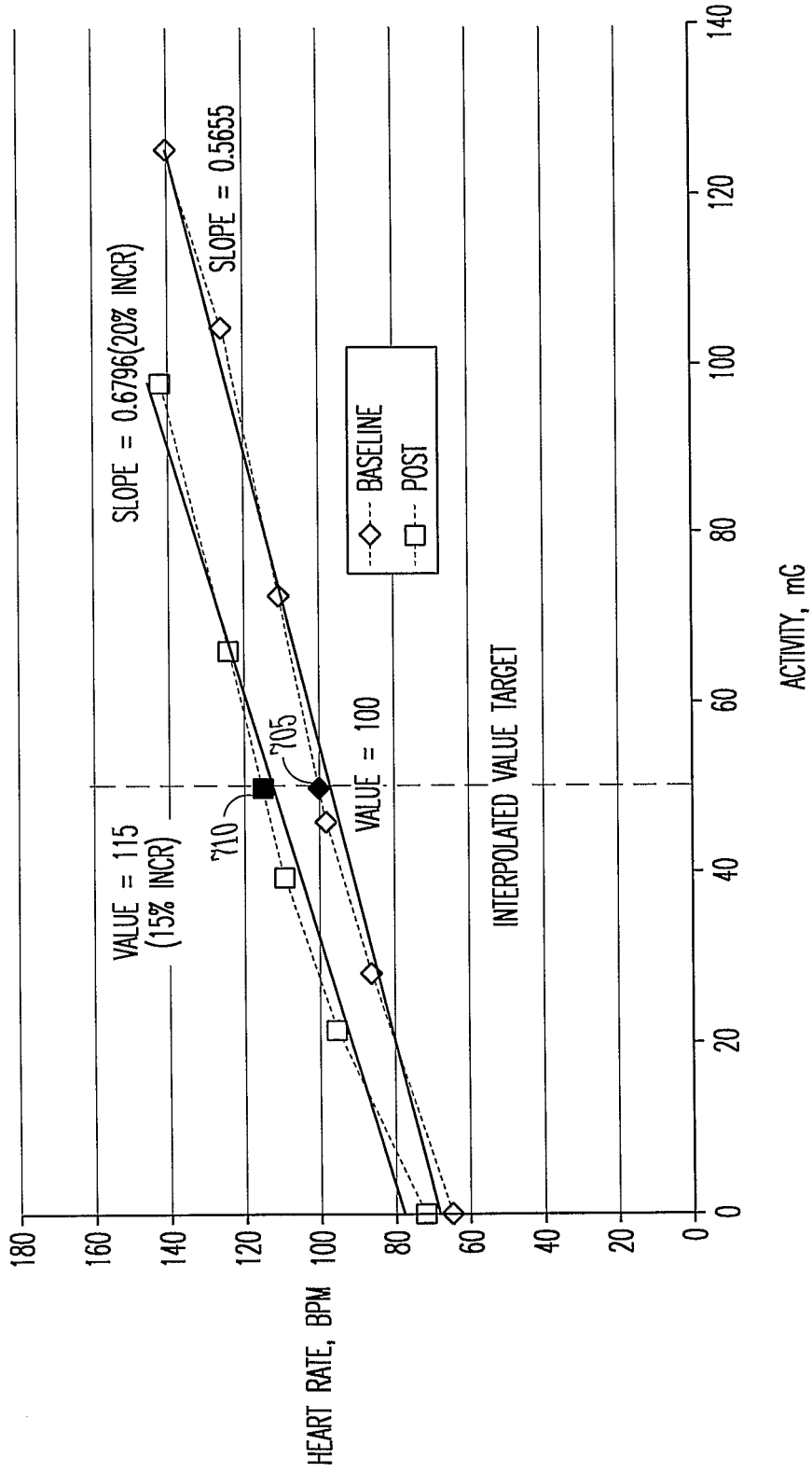


FIG. 7B

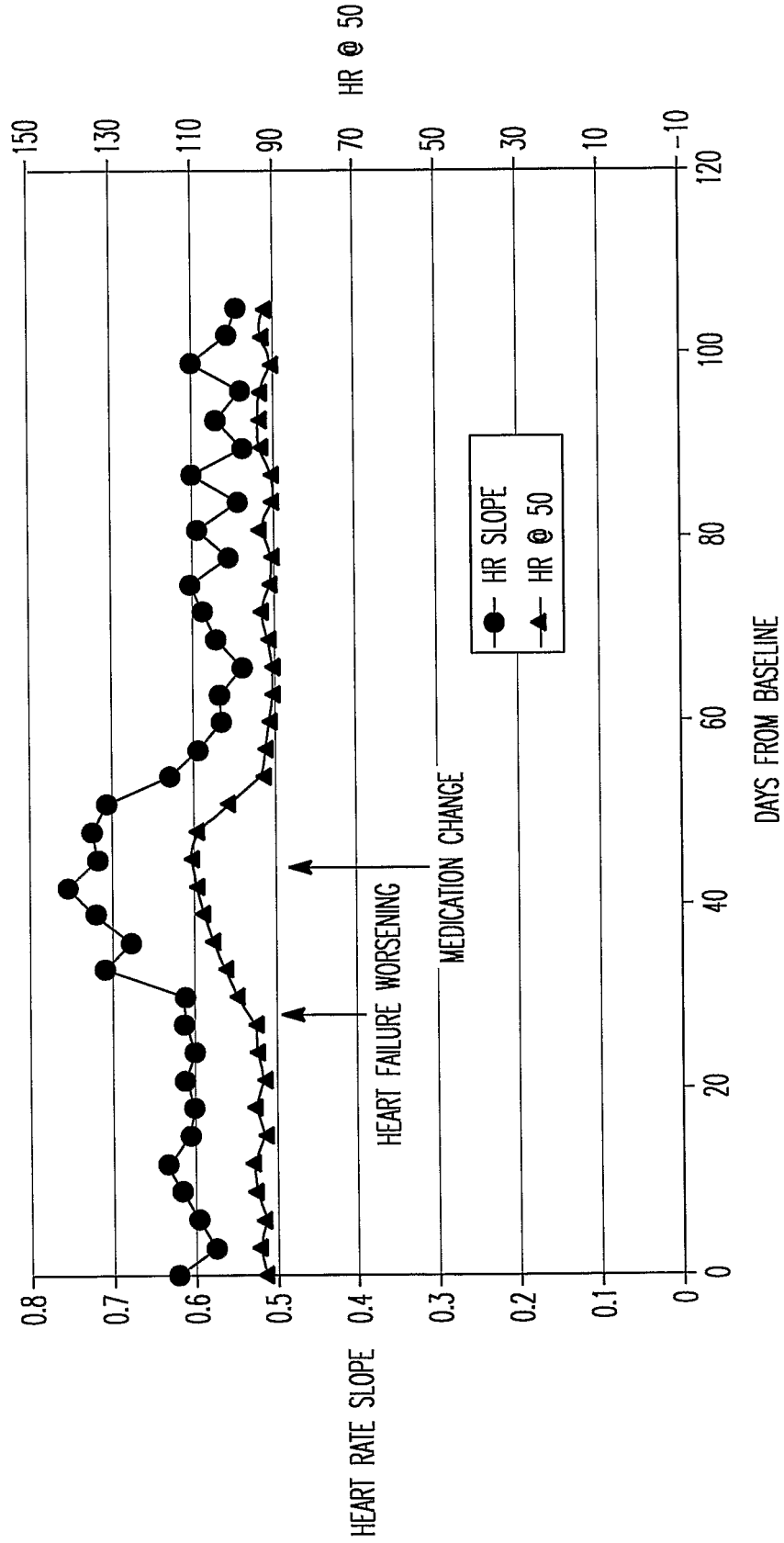


FIG. 8

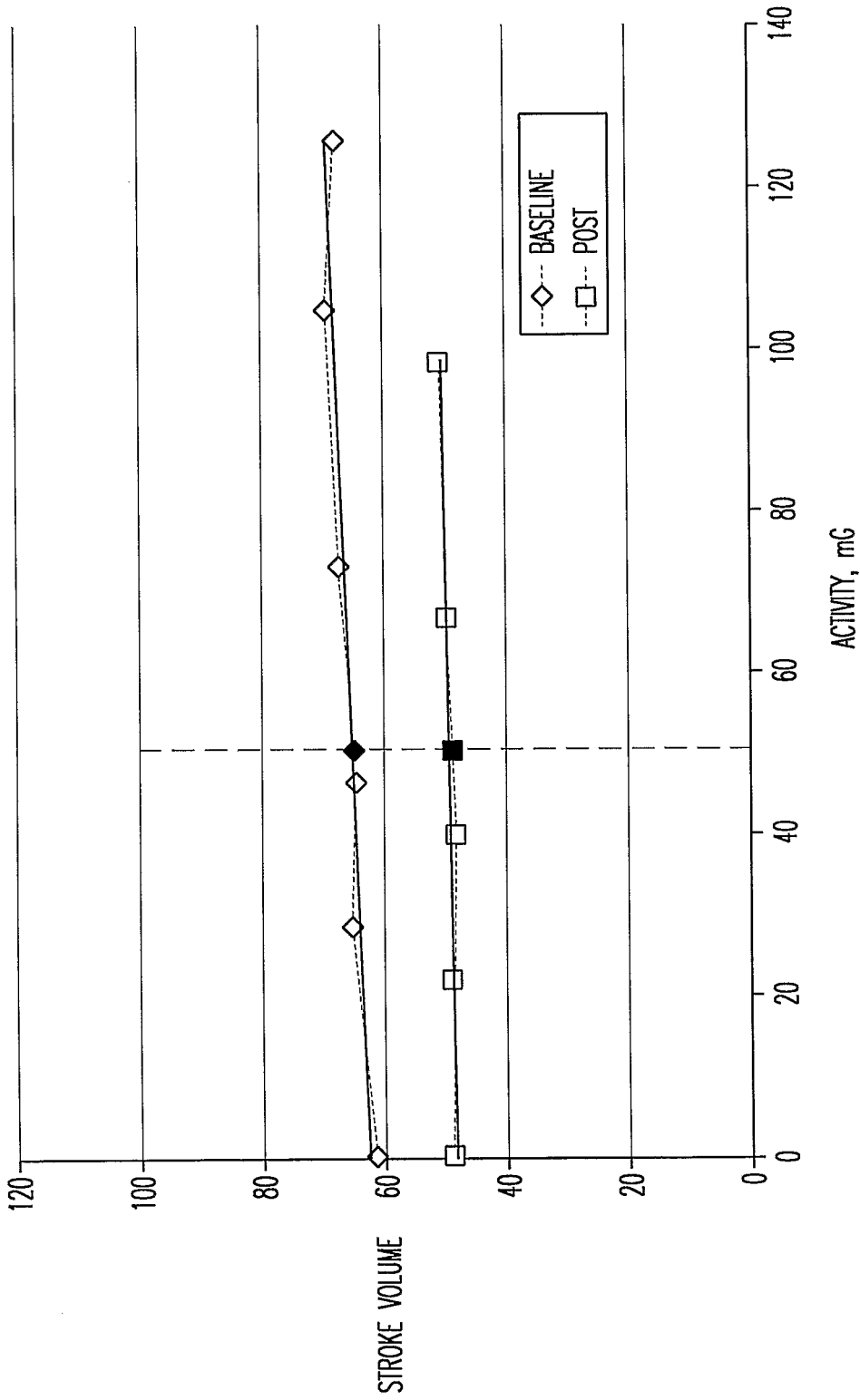


FIG. 9

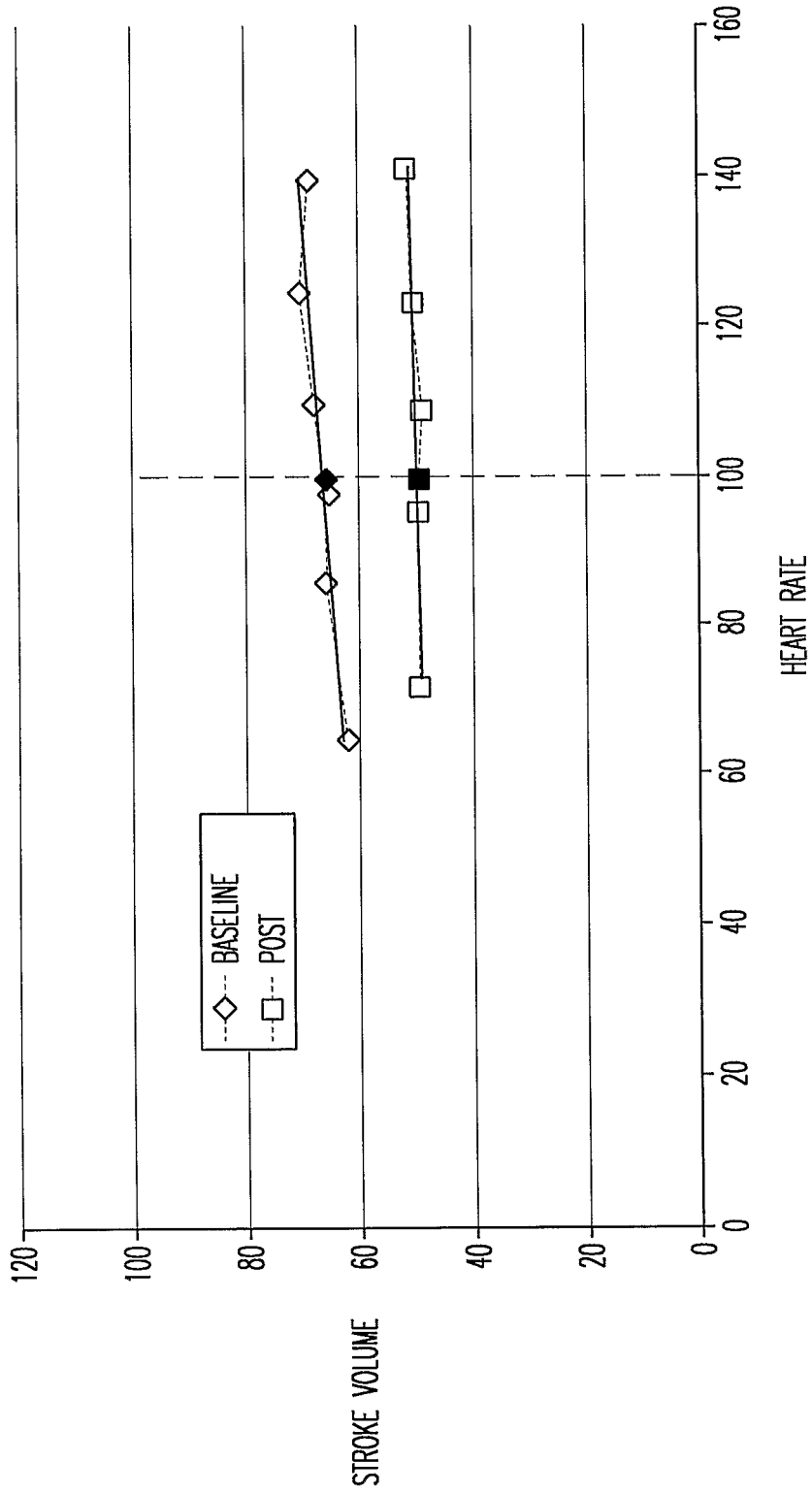


FIG. 10

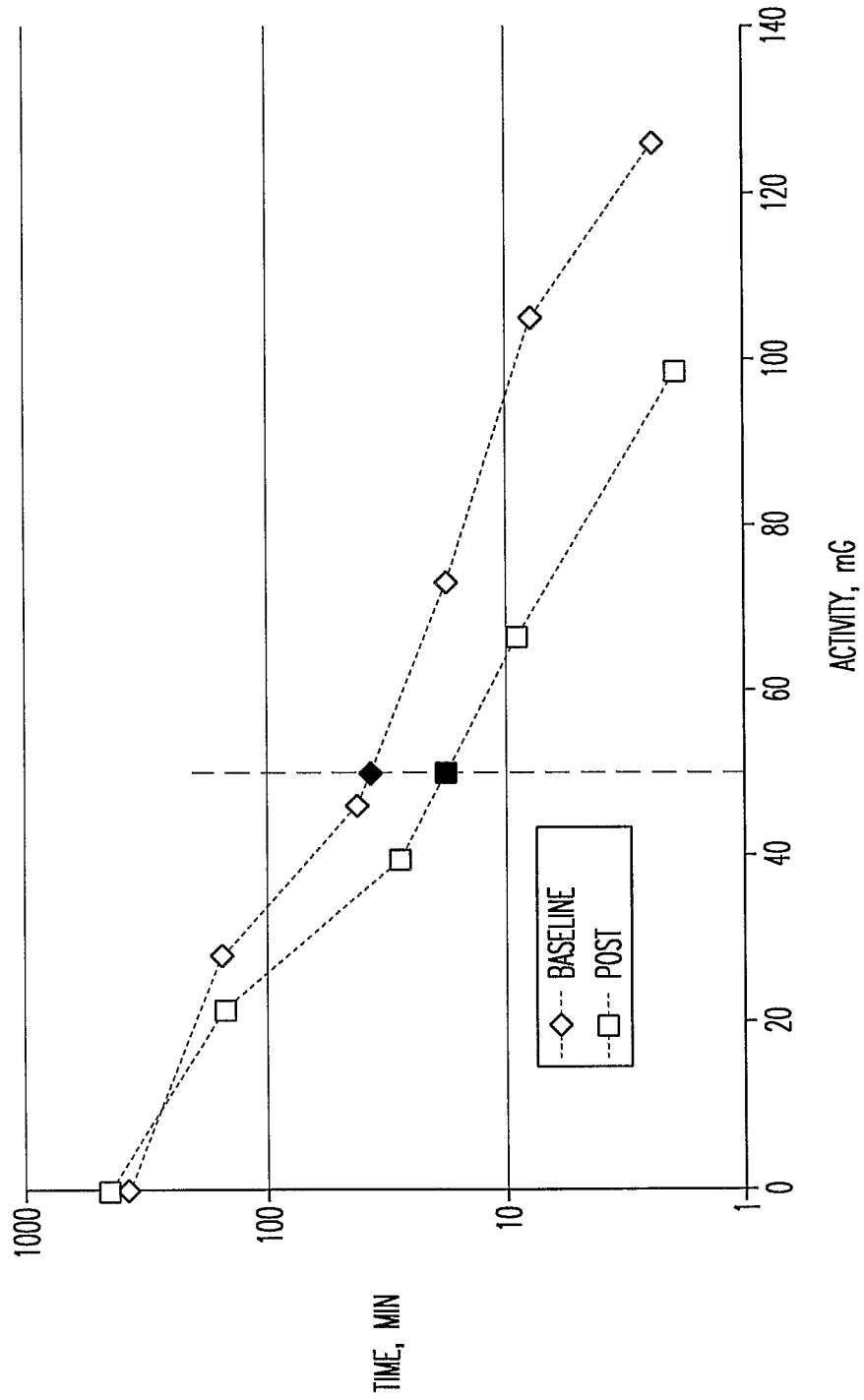


FIG. 11

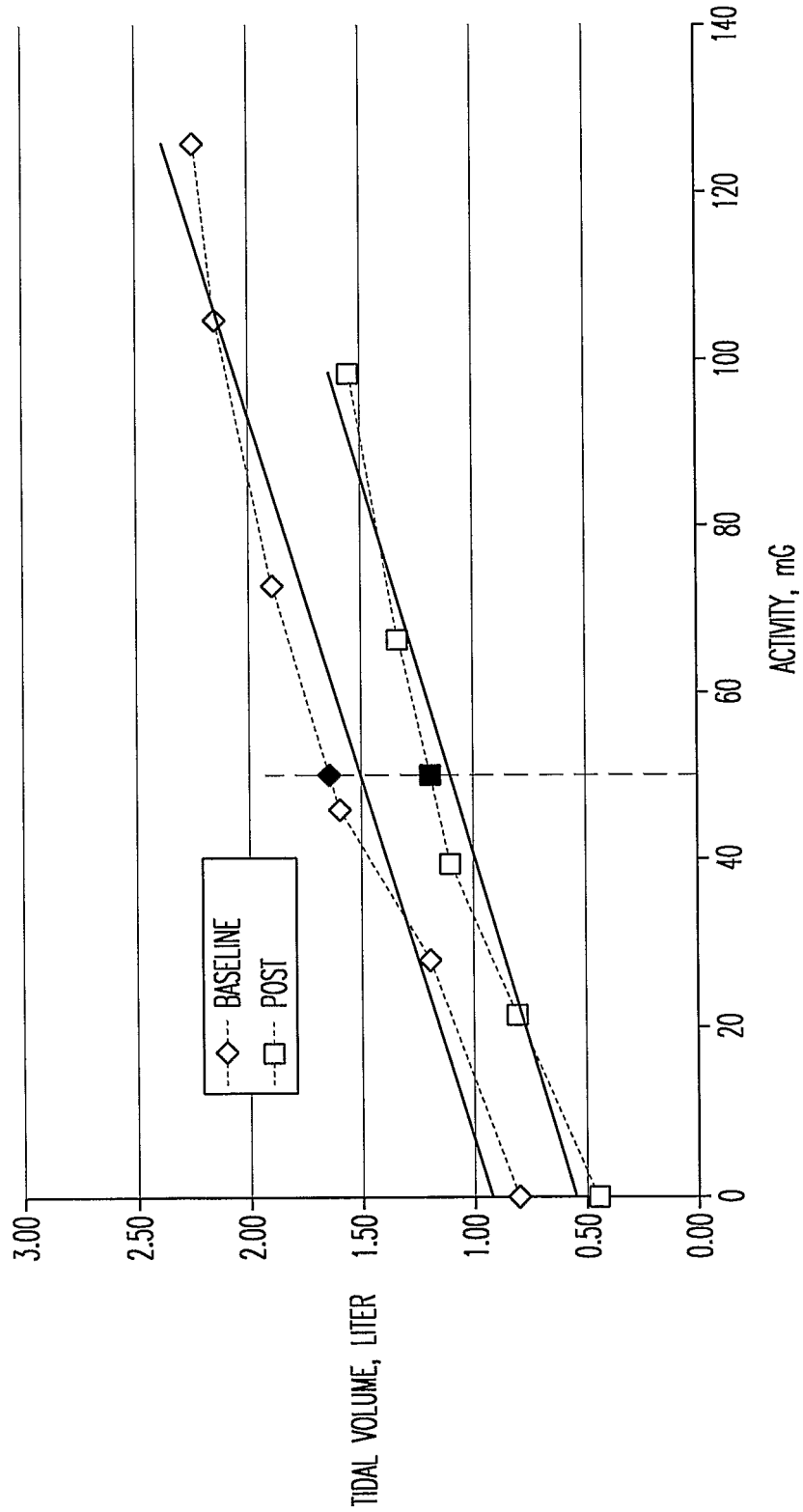


FIG. 12

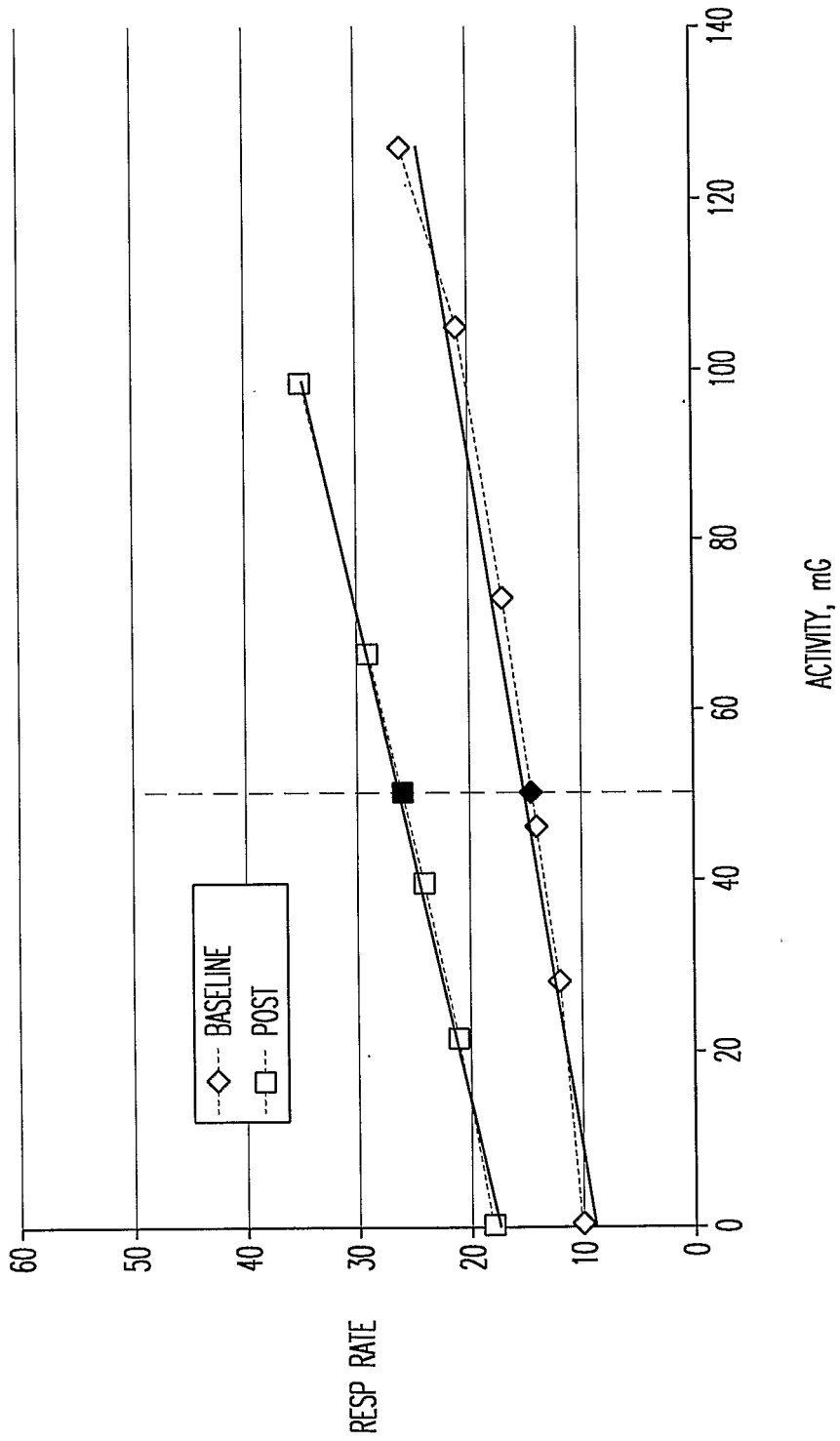


FIG. 13

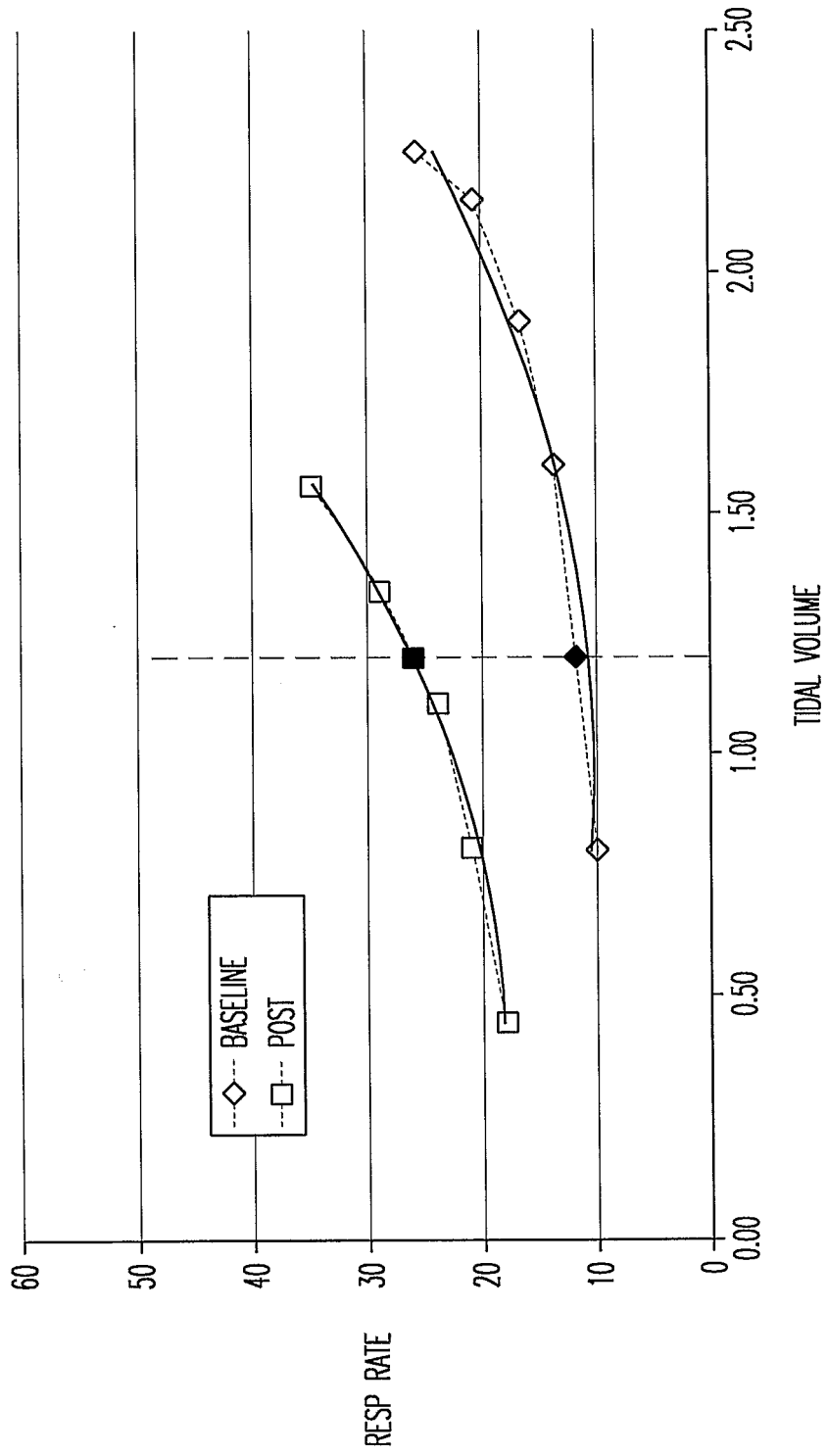


FIG. 14

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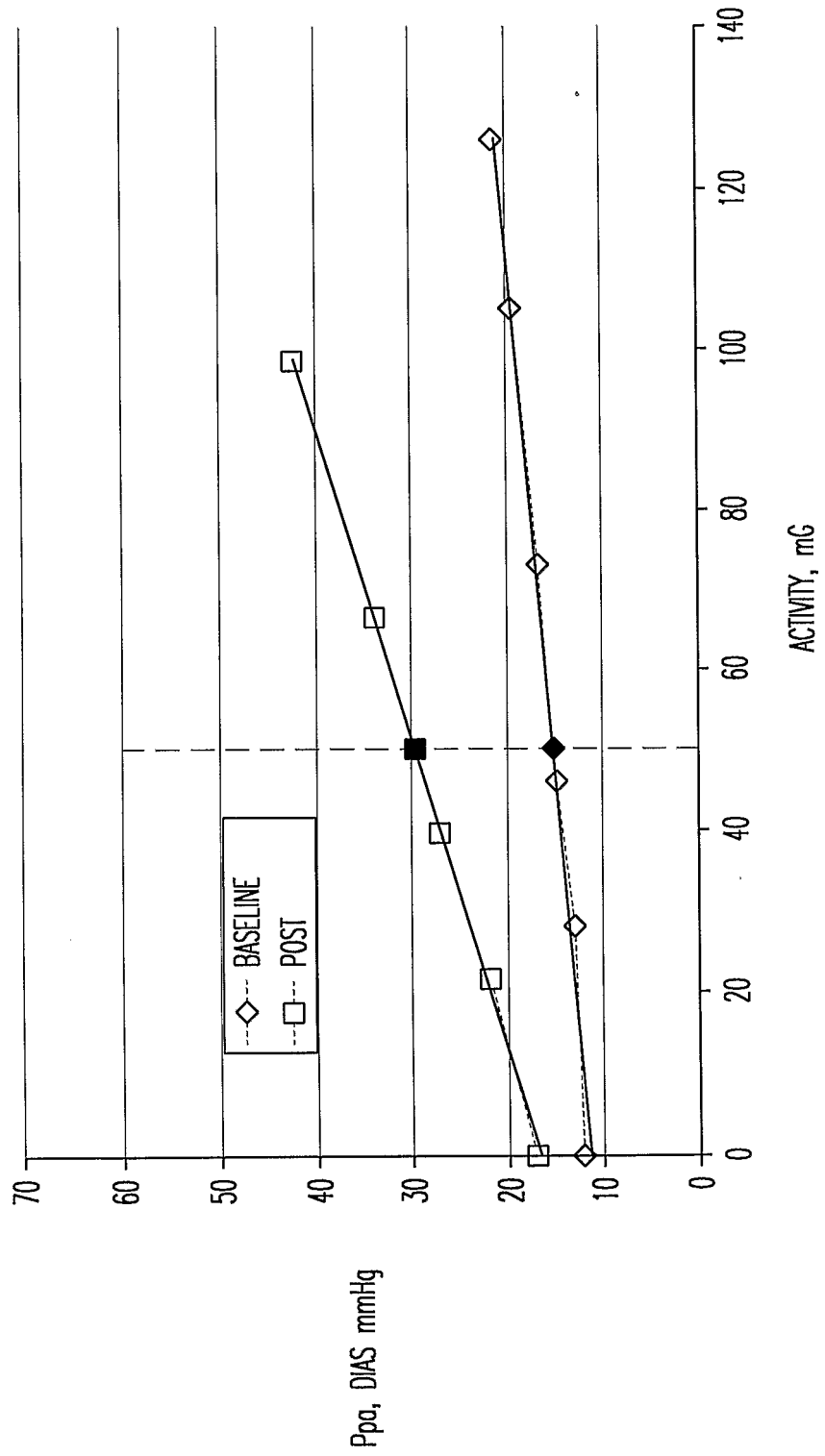


FIG. 15

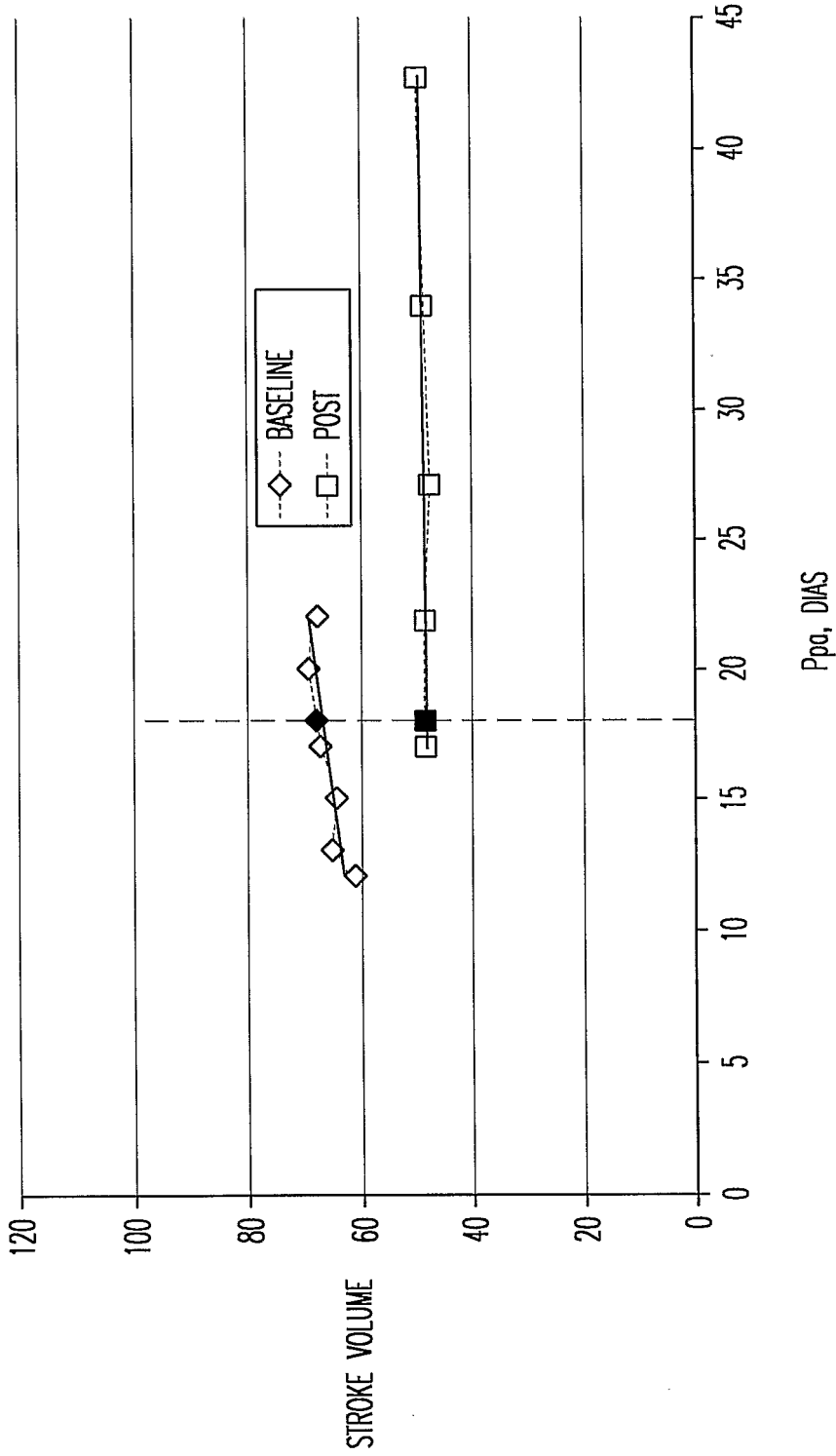


FIG. 16

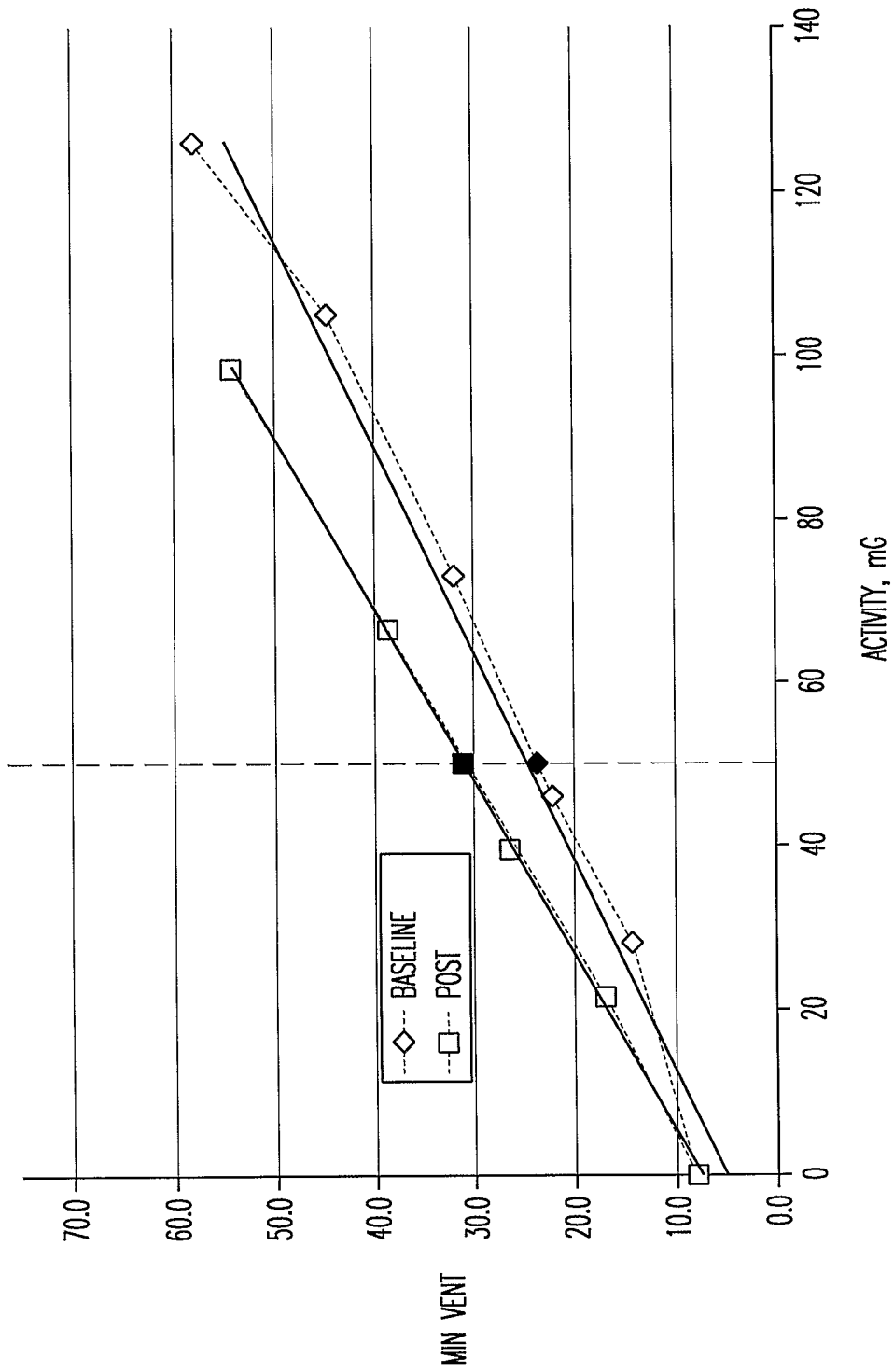


FIG. 17

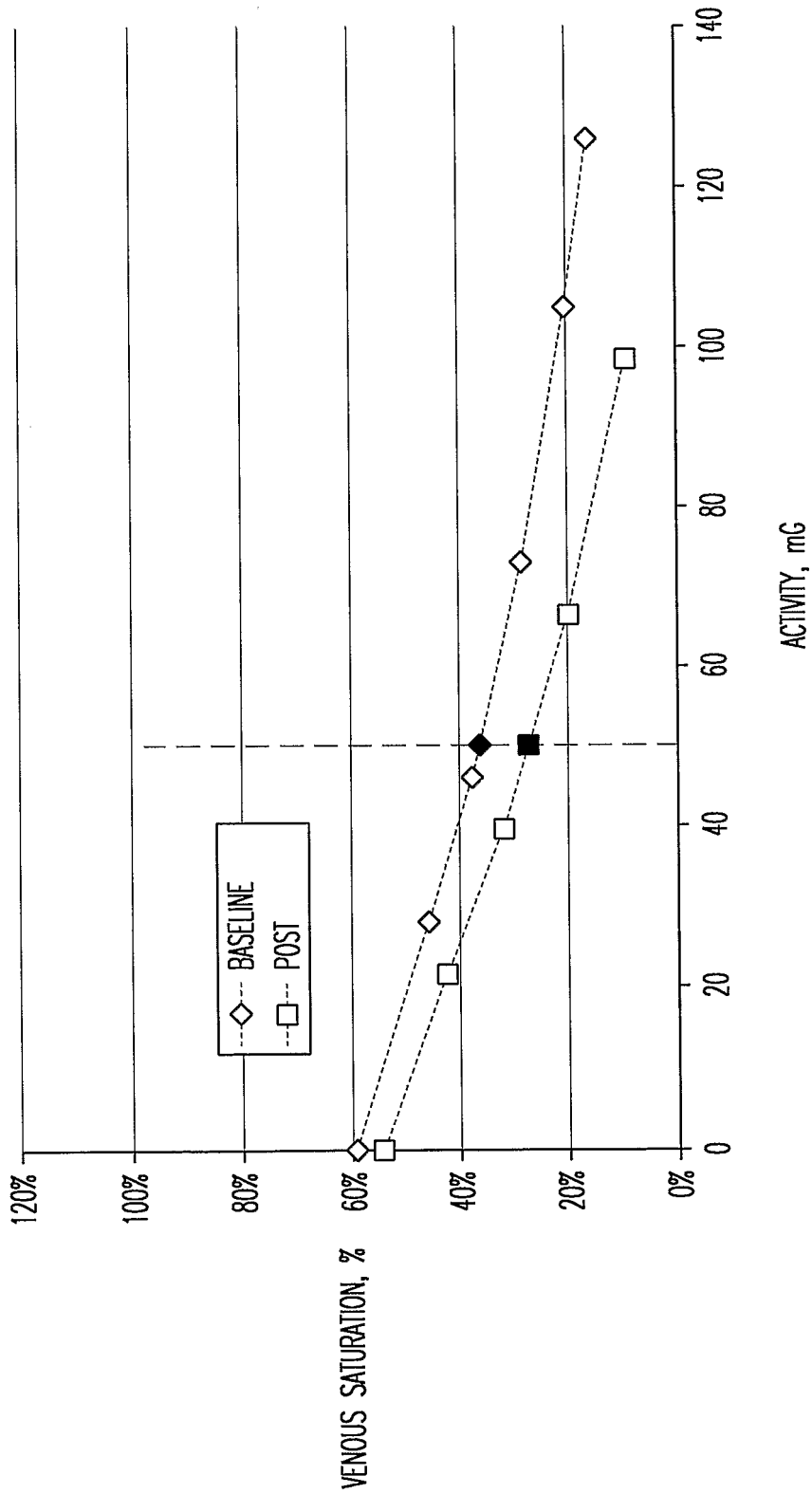


FIG. 18

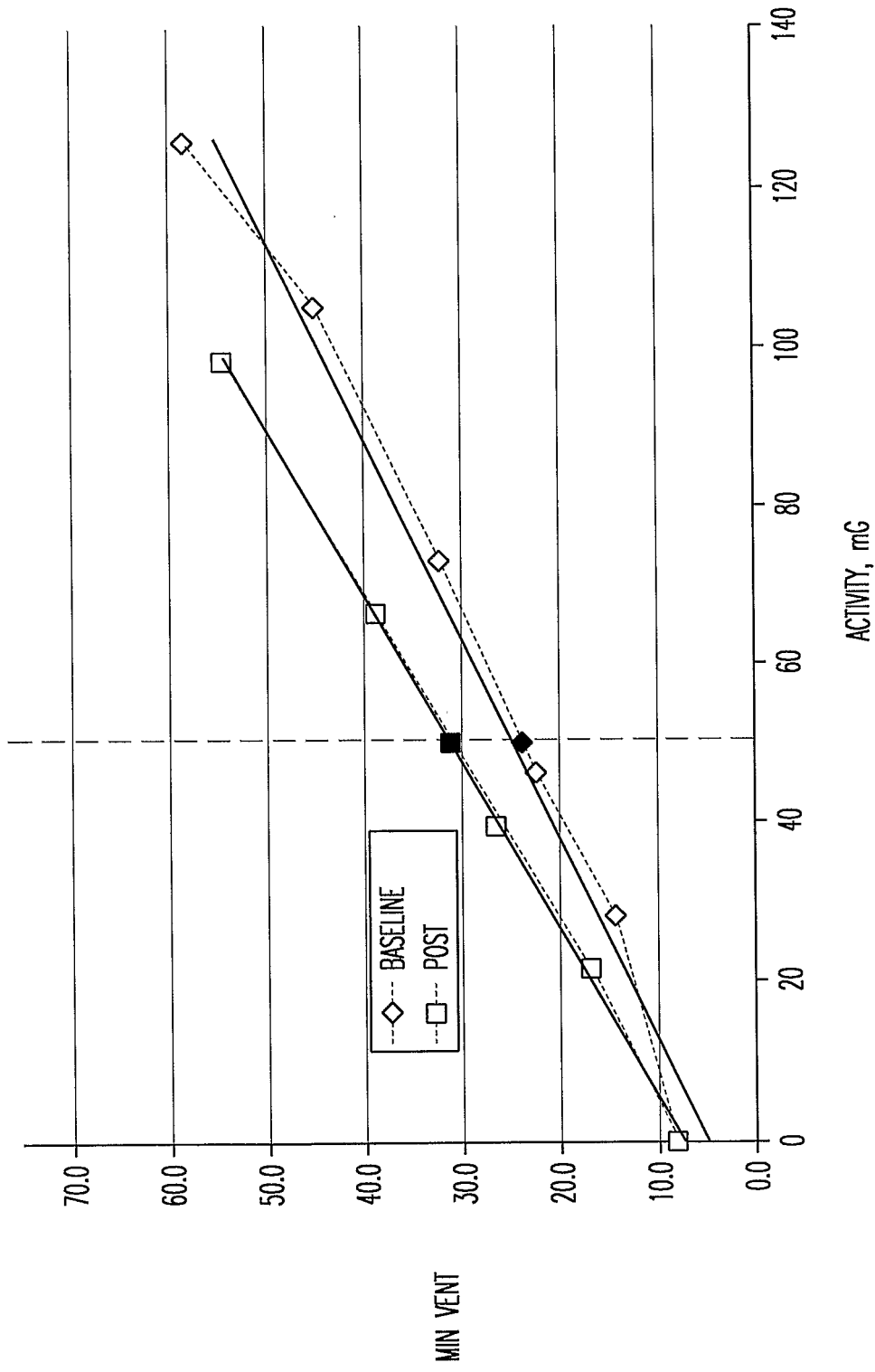


FIG. 19

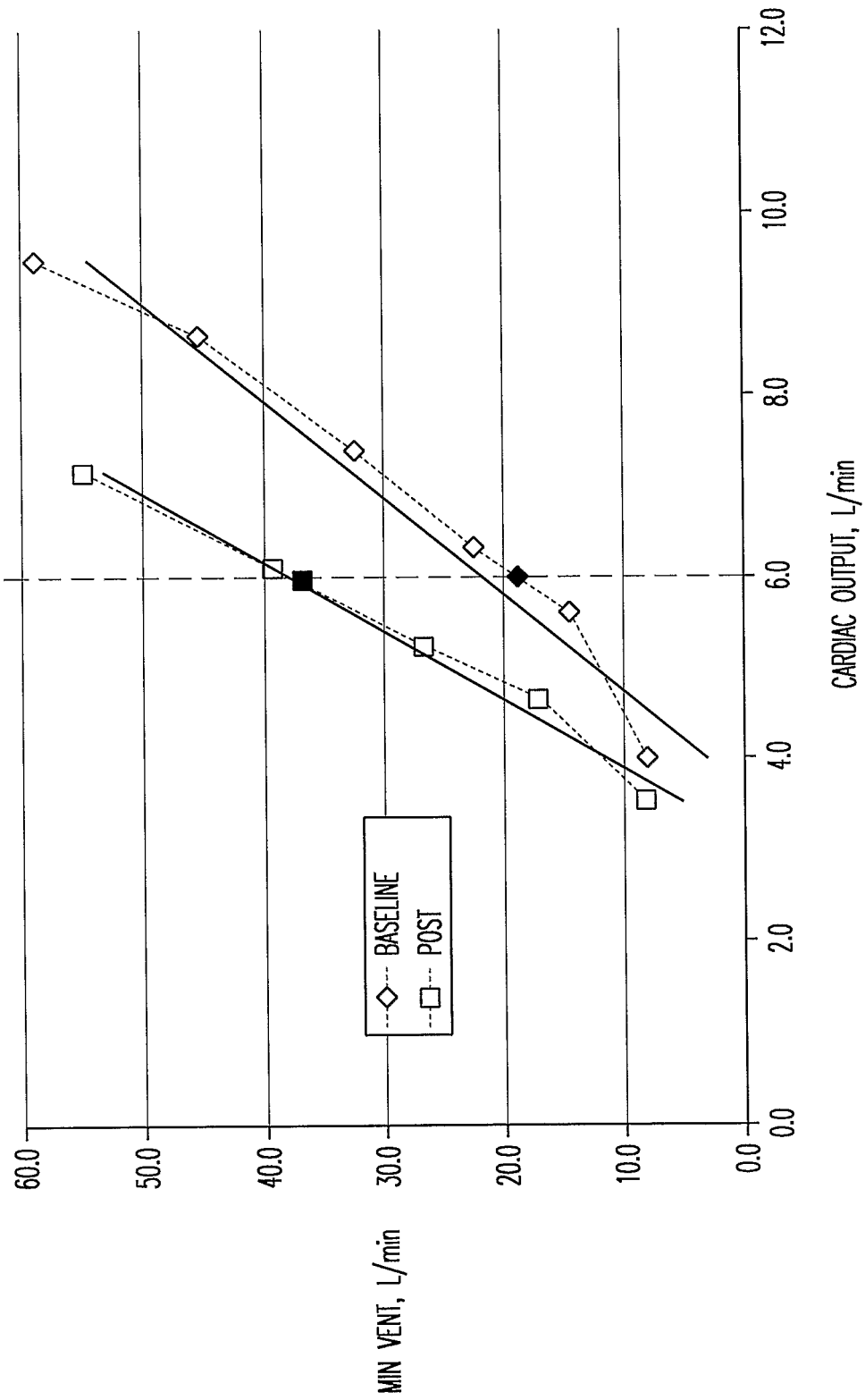


FIG. 20

INTERNATIONAL SEARCH REPORT

International application No PCT/US2006/026660

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61N1/37 A61N1/365 A61B5/0205 A61B5/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 A61N A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 904 313 B1 (SNELL JEFFERY D [US]) 7 June 2005 (2005-06-07) the whole document	1-4, 10-14, 19,26, 39,44
Y	US 2003/149453 A1 (KROLL MARK W [US] ET AL) 7 August 2003 (2003-08-07) the whole document	1-4, 10-14, 19,26, 39,44
A	US 2005/065443 A1 (TERNES DAVID [US]) 24 March 2005 (2005-03-24) the whole document	1-4,10, 14,19, 26,39,44
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

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- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search <p style="text-align: center;">1 November 2006</p>	Date of mailing of the international search report <p style="text-align: center;">10/11/2006</p>
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer <p style="text-align: center;">Ferrigno, Antonio</p>
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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/026660

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/23040 A (UAB RESEARCH FOUNDATION [US]; KAY G NEAL [US]; HOPPER DONALD L [US]; H) 5 April 2001 (2001-04-05) the whole document -----	1, 14, 19, 26, 39, 44
A	US 2003/204147 A1 (CONDIE CATHERINE R [US] ET AL) 30 October 2003 (2003-10-30) the whole document -----	1, 14, 19, 26, 39, 44
A	WO 2005/037077 A2 (INSPIRATION MEDICAL INC [US]; TEHRANI AMIR J [US]) 28 April 2005 (2005-04-28) the whole document -----	1, 14, 19, 26, 39, 44

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2006/026660

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6904313	B1	07-06-2005	NONE

US 2003149453	A1	07-08-2003	NONE

US 2005065443	A1	24-03-2005	NONE

WO 0123040	A	05-04-2001	AU 7713000 A 30-04-2001 US 6411850 B1 25-06-2002

US 2003204147	A1	30-10-2003	WO 03092803 A2 13-11-2003

WO 2005037077	A2	28-04-2005	DE 112004001953 T5 26-10-2006 DE 112004001954 T5 26-10-2006 DE 112004001957 T5 31-08-2006 US 2006030894 A1 09-02-2006 US 2006036294 A1 16-02-2006 US 2005085865 A1 21-04-2005 US 2005085866 A1 21-04-2005 US 2005085867 A1 21-04-2005 US 2005085868 A1 21-04-2005 US 2005085869 A1 21-04-2005 US 2005085734 A1 21-04-2005 WO 2005037172 A2 28-04-2005 WO 2005037366 A1 28-04-2005 WO 2005037220 A2 28-04-2005 WO 2005037173 A2 28-04-2005 WO 2005037174 A2 28-04-2005

专利名称(译)	监测对稳态活动的生理反应		
公开(公告)号	EP1909897A1	公开(公告)日	2008-04-16
申请号	EP2006786721	申请日	2006-07-07
[标]申请(专利权)人(译)	心脏起搏器股份公司		
申请(专利权)人(译)	心脏起搏器, INC.		
当前申请(专利权)人(译)	心脏起搏器, INC.		
[标]发明人	BECK KENNETH BAKER LEMONT HOPPER DONALD		
发明人	BECK, KENNETH BAKER, LEMONT HOPPER, DONALD		
IPC分类号	A61N1/37 A61N1/365 A61B5/0205 A61B5/11 A61B5/0245 A61B5/00 A61B5/0215 A61B5/029 A61B5/08 A61B5/145		
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优先权	11/184327 2005-07-19 US		
其他公开文献	EP1909897B1		
外部链接	Espacenet		

摘要(译)

系统和方法监测对稳态活动的生理反应。在一个示例中,使用可植入医疗设备从人或动物对象检测身体活动信号。还使用可植入医疗装置从受试者检测到不同的其他生理信号。处理身体活动信号以定义与受试者的第一和第二稳态身体活动水平相关联的第一和第二时间段。通过组合来自在第一时间段期间获得的其他生理信号的数据来获得第一指示符。通过组合来自在第二时间段期间获得的其他生理信号的数据来获得第二指示符。使用第一和第二指示符提供结果指示符。