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(54) **Title**: METHOD AND SYSTEM FOR IMPROVED ESTIMATION OF TIME OF LEFT VENTRICULAR PACING WITH RESPECT TO INTRINSIC RIGHT VENTRICULAR ACTIVATION IN CARDIAC RESYNCHRONIZATION THERAPY

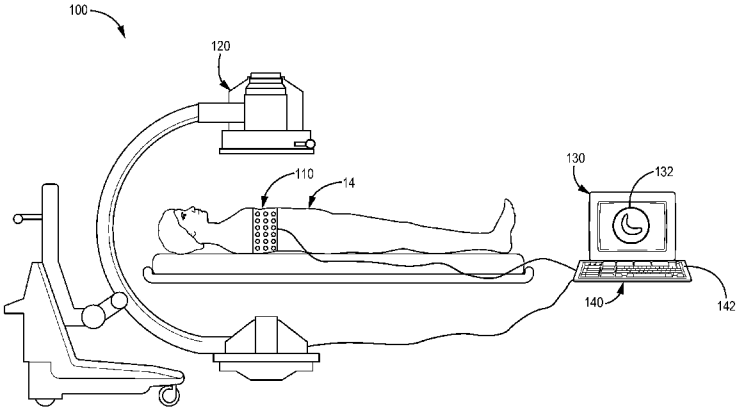

Fig. 1

(57) **Abstract**: A method and system of cardiac pacing is disclosed. A baseline rhythm is determined which includes a baseline atrial event and a baseline right ventricular RV event from an implanted cardiac lead or a leadless device, a pre-excitation interval determined from the baseline atrial event and the baseline RV event, and a plurality of activation times determined from a plurality of body-surface electrodes. A determination is made as to whether a time interval measured from an atrial event to a RV event is disparate from another time interval measured from the atrial event to an earliest RV activation time of the plurality of activation times. A correction factor is applied to the pre-excitation interval to obtain a corrected pre-excitation interval in response to determining the RV event is disparate from the earliest RV activation time.

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METHOD AND SYSTEM FOR IMPROVED ESTIMATION OF TIME OF LEFT VENTRICULAR PACING WITH RESPECT TO INTRINSIC RIGHT VENTRICULAR ACTIVATION IN CARDIAC RESYNCHRONIZATION THERAPY

TECHNICAL FIELD

The disclosure relates to electrophysiology and, more particularly, to adjusting the timing of the delivery of left ventricular pacing pulses in response to obtaining an objective estimate of the earliest intrinsic right ventricular activation.

BACKGROUND

The beat of the heart is controlled by the sinoatrial node, a group of conductive cells located in the right atrium near the entrance of the superior vena cava. The depolarization signal generated by the sinoatrial node activates the atrioventricular node. The atrioventricular node briefly delays the propagation of the depolarization signal, allowing the atria to drain, before passing the depolarization signal to the ventricles of the heart. The coordinated contraction of both ventricles drives the flow of blood through the body of a patient. In certain circumstances, the conduction of the depolarization signal from the atrioventricular node to the left and right ventricles may be interrupted or slowed. This may result in a dyssynchrony in the contraction of the left and right ventricles, which may lead to heart failure or death.

Cardiac resynchronization therapy (CRT) may correct the symptoms of electrical dyssynchrony by providing pacing therapy through medical electrical leads to one or both ventricles or atria to encourage earlier activation of the left or right ventricles. By pacing the contraction of the ventricles, the ventricles may be controlled so that the ventricles contract in synchrony. One form of CRT is fusion pacing. Fusion pacing typically involves left ventricle (LV) only pacing with an electrode on the LV medical electrical lead in coordination with the intrinsic right ventricle (RV) activation. Effective fusion requires, for example, that the timing of the LV pacing be in synchrony with the earliest activation on the RV chamber. Fusion pacing can also involve pacing the RV with an electrode on the RV medical electrical lead in coordination with the intrinsic LV activation; however, RV

only pacing is avoided because it can be arrhythmogenic in some patients and LV heart failure is more common than RV heart failure..

Achieving a positive clinical benefit from CRT is dependent on several therapy control parameters including the relative timing of pacing pulses delivered to effectively capture the right or left ventricles. Presently, CRT algorithms rely on a pre-excitation interval (e.g. 50-60 milliseconds (ms)). Pre-excitation interval is the time-interval that occurs before RV sensing in which pacing pulses are delivered to the LV. Conventional CRT algorithms do not take into consideration the fact that physicians may not consistently place the RV lead in the same or similar location for each patient. Consequently, in some cases, the RV sense time may significantly differ from the time of the onset of activation or the time of the earliest activation. For example, if the RV lead is in an electrically late area (e.g. RVOT), the time of the onset of activation occurs late (e.g. 70-80 ms after onset of depolarization). The timing of the delivery of LV pacing is calculated as 70-80 ms minus 50-60 ms which means the pacing stimulus can be delivered at 20-30 ms after onset of depolarization. The QRS complex on an electrocardiogram or an electrogram represents a summation of the advancing depolarization wavefronts through the ventricles. Pacing into the QRS complex or after onset of the QRS complex is not ideal for effective capture and does not provide the patient with full benefit of CRT. It is therefore desirable to develop additional methods or systems that are able to address the limitations associated with conventional CRT algorithms.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a diagram of an exemplary system including electrode apparatus, imaging apparatus, display apparatus, and computing apparatus.

FIG. 2 is an exemplary graphical user interface depicting mechanical motion data of a portion of a patient's heart.

FIGS. 3A-3B are diagrams of exemplary external electrode apparatus for measuring torso-surface potentials.

FIG. 4 is a diagram of exemplary surface locations of a patient mapped to implantation site regions of the patient's heart.

FIG. 5 is a flowchart of an exemplary method that uses a correction factor to a pre-excitation interval in response to determining a time interval ($T_{atrial\text{-}RV}$) measured from an atrial event to a RV sense time is disparate from another time interval ($T_{atrial\ -earliest\ RVAT}$).

FIG. 6 is a flowchart of an exemplary method that uses a correction factor to a pre-excitation interval in response to determining a substantially large offset exists between between the intrinsic rhythm activation time (T2) of an electrode selected from a plurality of surface electrodes and an earliest time of RV activation (T1) in intrinsic rhythm.

FIG. 7 is a diagram of an exemplary system including an exemplary implantable medical device (IMD).

FIG. 8A is a diagram of the exemplary IMD of FIG. 7.

FIG. 8B is a diagram of an enlarged view of a distal end of the electrical lead disposed in the left ventricle of FIG. 8A.

FIG. 9A is a block diagram of an exemplary IMD, e.g., the IMD of FIGS. 7-9.

FIG. 9B is another block diagram of an exemplary IMD (e.g., an implantable pulse generator) circuitry and associated leads employed in the system of FIGS. 7-9 for providing three sensing channels and corresponding pacing channels.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

The present disclosure is directed to a method and system that optimizes a form of cardiac resynchronization therapy (CRT) referred to as fusion pacing. In particular, the present disclosure sets the timing of the delivery of left ventricular pacing for fusion pacing in response to obtaining an objective estimate of the earliest intrinsic right ventricular activation. One or more embodiments begins by determining a baseline rhythm through a plurality of body-surface electrodes. A baseline rhythm may constitute RV only pacing or an intrinsic rhythm of the heart.

The left ventricle (LV) is not paced when obtaining the baseline rhythm. Heart activity is sensed through one or more implanted electrodes and/or surface electrodes A signal acquired or sensed from a single implanted electrode with respect to a distant electrode produces a unipolar electrogram (EGM) waveform while a signal acquired or sensed from a single surface electrode with respect to a indifferent electrode or composite reference like Wilson Central Terminal, produces a unipolar electrocardiogram (ECG). EGM signals and/or ECG signals are recorded during no pacing in the left ventricle (LV).

The baseline rhythm includes a variety of data. Exemplary data can include a baseline atrial event time and a baseline right ventricular (RV) sense time acquired from an implanted cardiac lead or a leadless device, a pre-excitation interval determined from the baseline atrial event time, the baseline RV sense time, and a plurality of electrical activation times determined from a plurality of body-surface electrodes. RV sense time includes RV events that are sensed such as an RV pace or an intrinsic RV event. A determination is made as to whether a time interval ($T_{atrial\text{-}RV}$) measured from an atrial event to a RV sense time is disparate from another time interval ($T_{atrial\text{ -earliest RVAT}}$) measured from the atrial event to an earliest RV activation time of the plurality of activation times. Disparate is defined such that the earliest RV activation time is about 40-300 ms ahead of the earliest RV sense time. In response to determining that the $T_{atrial\text{-}RV}$ is disparate from the $T_{atrial\text{ -earliest RVAT}}$, a correction factor is then applied to the pre-excitation interval to obtain, and store into memory, a corrected pre-excitation interval. The processor is then configured to signal the pulse generator to deliver electrical stimuli to a LV using the corrected pre-excitation interval before RV sensing time. The method and system described herein improves a patient's response to CRT by accurately and reliably timing the delivery of LV pacing with respect to RV sensing.

In the following detailed description of illustrative embodiments, reference is made to the accompanying figures of the drawing which form a part hereof, and in which are shown, by way of illustration, specific embodiments which may be practiced. It is to be understood that other embodiments may be utilized and

structural changes may be made without departing from (e.g., still falling within) the scope of the disclosure presented hereby.

Exemplary systems, apparatus, and methods shall be described with reference to Figures 1-9B. It will be apparent to one skilled in the art that elements or processes from one embodiment may be used in combination with elements or processes of the other embodiments, and that the possible embodiments of such methods, apparatus, and systems using combinations of features set forth herein is not limited to the specific embodiments shown in the Figures and/or described herein. Further, it will be recognized that the embodiments described herein may include many elements that are not necessarily shown to scale. Still further, it will be recognized that timing of the processes and the size and shape of various elements herein may be modified but still fall within the scope of the present disclosure, although certain timings, one or more shapes and/or sizes, or types of elements, may be advantageous over others.

From unipolar electrocardiogram (ECG) recordings, electrical activation times can be detected or estimated in proximity of a reference location (e.g., which can be a chosen location for the left ventricle lead during implant). Such electrical activation times may be measured and displayed, or conveyed, to an implanter by a system which acquires the ECG signals and generates the metric of electrical activation (e.g., q-LV) time.

As described herein, various exemplary systems, methods, and interfaces may be configured to use electrode apparatus including external electrodes, imaging apparatus, display apparatus, and computing apparatus to noninvasively assist a user (e.g., a physician) in selecting one or more locations (e.g., implantation site regions) proximate a patient's heart for one or more implantable electrodes and/or to navigate one or more implantable electrodes to the selected location(s). An exemplary system 100 including electrode apparatus 110, imaging apparatus 120, display apparatus 130, and computing apparatus 140 is depicted in FIG. 1.

The electrode apparatus 110 as shown includes a plurality of electrodes incorporated, or included within a band wrapped around the chest, or torso, of a patient 14. The electrode apparatus 110 is operatively coupled to the computing apparatus 140 (e.g., through one or wired electrical connections, wirelessly, etc.) to provide electrical signals from each of the electrodes to the computing apparatus 140 for analysis. Exemplary electrode apparatus 110 will be described in more detail in reference to FIGS. 3A-3B.

The imaging apparatus 120 may be any type of imaging apparatus configured to image, or provide images of, at least a portion of the patient in a non-invasive manner. For example, the imaging apparatus 120 may not use any components or parts that may be located within the patient to provide images of at least a portion of the patient except non-invasive tools such as contrast solution. It is to be understood that the exemplary systems, methods, and interfaces described herein may noninvasively assist a user (e.g., a physician) in selecting a location proximate a patient's heart for an implantable electrode, and after the exemplary systems, methods, and interfaces have provided noninvasive assistance, the exemplary systems, methods, and interfaces may then provide assistance to implant, or navigate, an implantable electrode into the patient, e.g., proximate the patient's heart.

For example, after the exemplary systems, methods, and interfaces have provided noninvasive assistance, the exemplary systems, methods, and interfaces may then provide image guided navigation that may be used to navigate leads including electrodes, leadless electrodes, wireless electrodes, catheters, etc., within the patient's body. Further, although the exemplary systems, methods, and interfaces are described herein with reference to a patient's heart, it is to be understood that the exemplary systems, methods, and interfaces may be applicable to any other portion of the patient's body.

The imaging apparatus 120 may be configured to capture, or take, x-ray images (e.g., two dimensional x-ray images, three dimensional x-ray images, etc.) of the patient 14. The imaging apparatus 120 may be operatively coupled (e.g.,

through one or wired electrical connections, wirelessly, etc.) to the computing apparatus 140 such that the images captured by the imaging apparatus 120 may be transmitted to the computing apparatus 140. Further, the computing apparatus 140 may be configured to control the imaging apparatus 120 to, e.g., configure the imaging apparatus 120 to capture images, change one or more settings of the imaging apparatus 120, etc.

It will be recognized that while the imaging apparatus 120 as shown in FIG. 1 may be configured to capture x-ray images, any other alternative imaging modality may also be used by the exemplary systems, methods, and interfaces described herein. For example, the imaging apparatus 120 may be configured to capture images, or image data, using isocentric fluoroscopy, bi-plane fluoroscopy, ultrasound, computed tomography (CT), multi-slice computed tomography (MSCT), magnetic resonance imaging (MRI), high frequency ultrasound (HIFU), optical coherence tomography (OCT), intra-vascular ultrasound (IVUS), two dimensional (2D) ultrasound, three dimensional (3D) ultrasound, four dimensional (4D) ultrasound, intraoperative CT, intraoperative MRI, etc. Further, it is to be understood that the imaging apparatus 120 may be configured to capture a plurality of consecutive images (e.g., continuously) to provide video frame data. In other words, a plurality of images taken over time using the imaging apparatus 120 may provide motion picture data. Additionally, the images may also be obtained and displayed in two, three, or four dimensions. In more advanced forms, four-dimensional surface rendering of the heart or other regions of the body may also be achieved by incorporating heart data or other soft tissue data from an atlas map or from pre-operative image data captured by MRI, CT, or echocardiography modalities. Image datasets from hybrid modalities, such as positron emission tomography (PET) combined with CT, or single photon emission computer tomography (SPECT) combined with CT, could also provide functional image data superimposed onto anatomical data to be used to confidently reach target locations within the heart or other areas of interest.

The display apparatus 130 and the computing apparatus 140 may be configured to display and analyze data such as, e.g., surrogate electrical activation data, image data, mechanical motion data, etc. gathered, or collected, using the electrode apparatus 110 and the imaging apparatus 120 to noninvasively assist a user in location selection of an implantable electrode. In at least one embodiment, the computing apparatus 140 may be a server, a personal computer, or a tablet computer. The computing apparatus 140 may be configured to receive input from input apparatus 142 and transmit output to the display apparatus 130. Further, the computing apparatus 140 may include data storage that may allow for access to processing programs or routines and/or one or more other types of data, e.g., for driving a graphical user interface configured to noninvasively assist a user in location selection of an implantable electrode, etc.

The computing apparatus 140 may be operatively coupled to the input apparatus 142 and the display apparatus 130 to, e.g., transmit data to and from each of the input apparatus 142 and the display apparatus 130. For example, the computing apparatus 140 may be electrically coupled to each of the input apparatus 142 and the display apparatus 130 using, e.g., analog electrical connections, digital electrical connections, wireless connections, bus-based connections, network-based connections, internet-based connections, etc. As described further herein, a user may provide input to the input apparatus 142 to manipulate, or modify, one or more graphical depictions displayed on the display apparatus 130 to view and/or select one or more target or candidate locations of a portion of a patient's heart as further described herein.

Although as depicted the input apparatus 142 is a keyboard, it is to be understood that the input apparatus 142 may include any apparatus capable of providing input to the computing apparatus 140 to perform the functionality, methods, and/or logic described herein. For example, the input apparatus 142 may include a mouse, a trackball, a touchscreen (e.g., capacitive touchscreen, a resistive touchscreen, a multi-touch touchscreen, etc.), etc. Likewise, the display apparatus 130 may include any apparatus capable of displaying information to a

user, such as a graphical user interface 132 including graphical depictions of anatomy of a patient's heart, images of a patient's heart, graphical depictions of locations of one or more electrodes, graphical depictions of one or more target or candidate locations, alphanumeric representations of one or more values, graphical depictions or actual images of implanted electrodes and/or leads, etc. For example, the display apparatus 130 may include a liquid crystal display, an organic light-emitting diode screen, a touchscreen, a cathode ray tube display, etc.

The graphical user interfaces 132 displayed by the display apparatus 130 may include, or display, one or more regions used to display graphical depictions, to display images, to allow selection of one or more regions or areas of such graphical depictions and images, etc. As used herein, a "region" of a graphical user interface 132 may be defined as a portion of the graphical user interface 132 within which information may be displayed or functionality may be performed. Regions may exist within other regions, which may be displayed separately or simultaneously. For example, smaller regions may be located within larger regions, regions may be located side-by-side, etc. Additionally, as used herein, an "area" of a graphical user interface 132 may be defined as a portion of the graphical user interface 132 located with a region that is smaller than the region it is located within.

The processing programs or routines stored and/or executed by the computing apparatus 140 may include programs or routines for computational mathematics, matrix mathematics, decomposition algorithms, compression algorithms (e.g., data compression algorithms), calibration algorithms, image construction algorithms, signal processing algorithms (e.g., Fourier transforms, fast Fourier transforms, etc.), standardization algorithms, comparison algorithms, vector mathematics, or any other processing required to implement one or more exemplary methods and/or processes described herein. Data stored and/or used by the computing apparatus 140 may include, for example, image data from the imaging apparatus 120, electrical signal data from the electrode apparatus 110,

graphics (e.g., graphical elements, icons, buttons, windows, dialogs, pull-down menus, graphic areas, graphic regions, 3D graphics, etc.), graphical user interfaces, results from one or more processing programs or routines employed according to the disclosure herein, or any other data that may be necessary for carrying out the one and/or more processes or methods described herein.

In one or more embodiments, the exemplary systems, methods, and interfaces may be implemented using one or more computer programs executed on programmable computers, such as computers that include, for example, processing capabilities, data storage (e.g., volatile or non-volatile memory and/or storage elements), input devices, and output devices. Program code and/or logic described herein may be applied to input data to perform functionality described herein and generate desired output information. The output information may be applied as input to one or more other devices and/or methods as described herein or as would be applied in a known fashion.

The one or more programs used to implement the systems, methods, and/or interfaces described herein may be provided using any programmable language, e.g., a high level procedural and/or object orientated programming language that is suitable for communicating with a computer system. Any such programs may, for example, be stored on any suitable device, e.g., a storage media, that is readable by a general or special purpose program running on a computer system (e.g., including processing apparatus) for configuring and operating the computer system when the suitable device is read for performing the procedures described herein. In other words, at least in one embodiment, the exemplary systems, methods, and/or interfaces may be implemented using a computer readable storage medium, configured with a computer program, where the storage medium so configured causes the computer to operate in a specific and predefined manner to perform functions described herein. Further, in at least one embodiment, the exemplary systems, methods, and/or interfaces may be described as being implemented by logic (e.g., object code) encoded in one or more non-transitory media that includes code for execution and, when executed

by a processor, is operable to perform operations such as the methods, processes, and/or functionality described herein.

The computing apparatus 140 may be, for example, any fixed or mobile computer system (e.g., a controller, a microcontroller, a personal computer, minicomputer, tablet computer, etc.). The exact configuration of the computing apparatus 130 is not limiting, and essentially any device capable of providing suitable computing capabilities and control capabilities (e.g., graphics processing, etc.) may be used. As described herein, a digital file may be any medium (e.g., volatile or non-volatile memory, a CD-ROM, a punch card, magnetic recordable tape, etc.) containing digital bits (e.g., encoded in binary, trinary, etc.) that may be readable and/or writeable by computing apparatus 140 described herein. Also, as described herein, a file in user-readable format may be any representation of data (e.g., ASCII text, binary numbers, hexadecimal numbers, decimal numbers, graphically, etc.) presentable on any medium (e.g., paper, a display, etc.) readable and/or understandable by a user.

In view of the above, it will be readily apparent that the functionality as described in one or more embodiments according to the present disclosure may be implemented in any manner as would be known to one skilled in the art. As such, the computer language, the computer system, or any other software/hardware which is to be used to implement the processes described herein shall not be limiting on the scope of the systems, processes or programs (e.g., the functionality provided by such systems, processes or programs) described herein.

As used herein, mechanical motion data may be defined as data relating to the mechanical motion of one or more regions of a patient's heart such as portions of the walls of the patient's heart. It may be desirable for target locations in a patient's heart for implantable electrode placement to also have late mechanical motion timing (e.g., later motion than other portions of the patient's heart, motion that is later than a selected threshold value or time, etc.). Mechanical motion data may be measured and determined using the exemplary imaging apparatus 120

and the computing apparatus 140. For example, a plurality of frames of image data may be captured using the imaging apparatus 120 and analyzed by the computing apparatus to determine mechanical motion information, or data, of one or more regions of a patient's heart.

Local 3D motion of the heart wall can be decomposed into two components: the first component expresses change of distances between neighboring points and is referenced as a strain (e.g., contraction, when distances decrease or expansion, when distances increase, etc.) and the second non-strain component may not involve change of distances between neighboring points and may involve translation and/or rotation. The strain may be anisotropic. Specifically, a circumferential strain when cross sections (segments) perpendicular to the long axis of a heart chamber change length may be differentiated from a longitudinal strain when lines substantially parallel to long axis change length. The exemplary imaging apparatus 120 described herein may be configured to provide image data to provide graphical depictions of contraction and expansion as a change in scale of a blood vessel tree, or in other words, as a change of distance between points, while rotation and translation are visualized without change of distances.

The imaging apparatus 120, which may be a computerized X-ray machine, may be directed at the patient's heart and activated to produce a time sequence of X-ray images of the heart area at the field of view. In order to expose blood vessels (e.g., such as the coronary vessels) at the heart area under view, the X-ray images may be preferably obtained under angiography procedure by injecting contrast agent to the patient. Where the vessels to be detected are the coronary veins, the angiography may be carried out after a balloon is inserted and inflated inside the vein, e. g., the coronary sinus, so as to prevent blood flow from dispersing the contrast agent before the images are taken.

For example, a time sequence of two-dimensional X-ray projection images may be captured by imaging apparatus of FIG. 1 and stored by the computing apparatus 140. The two-dimensional images may be angiograms taken after the

patient has been injected with contrast agent. The time sequence may include "snapshots" (e.g., angiographic cine-runs) of the coronary vessel under the same projection angle during at least part of the cardiac cycle of the patient. Further, the projection direction may be selected to be substantially orthogonal to the surface of the heart at the region of interest or to the main velocity component thereof.

The blood vessels of interest may be tracked through the time sequence of images in order to identify the movements of the vessels through at least part of the cardiac cycle. Tracking of blood vessels through the time sequence of images may be performed by calculation of local area transformations from one frame to the next, or by tracking selected control points in the detected vessels. Yet, in accordance with some embodiments, tracking the vessels may be performed by a hybrid combination of the two methods.

Examples of systems and/or imaging apparatus configured to capture and determine mechanical motion information may be described in U.S. Pat. App. Pub. No. 2005/0008210 to Evron et al. published on January 13, 2005, U.S. Pat. App. Pub. No. 2006/0074285 to Zarkh et al. published on April 6, 2006, U.S. Pat. App. Pub. No. 2011/0112398 to Zarkh et al. published on May 12, 2011, U.S. Pat. App. Pub. No. 2013/0116739 to Brada et al. published on May 9, 2013, U.S. Pat. No. 6,980,675 to Evron et al. issued on December 27, 2005, U.S. Pat. No. 7,286,866 to Okerlund et al. issued on October 23, 2007, U.S. Pat. No. 7,308,297 to Reddy et al. issued on December 11, 2011, U.S. Pat. No. 7,308,299 to Burrell et al. issued on December 11, 2011, U.S. Pat. No. 7,321,677 to Evron et al. issued on January 22, 2008, U.S. Pat. No. 7,346,381 to Okerlund et al. issued on March 18, 2008, U.S. Pat. No. 7,454,248 to Burrell et al. issued on November 18, 2008, U.S. Pat. No. 7,499,743 to Vass et al. issued on March 3, 2009, U.S. Pat. No. 7,565,190 to Okerlund et al. issued on July 21, 2009, U.S. Pat. No. 7,587,074 to Zarkh et al. issued on September 8, 2009, U.S. Pat. No. 7,599,730 to Hunter et al. issued on October 6, 2009, U.S. Pat. No. 7,613,500 to Vass et al. issued on November 3, 2009, U.S. Pat. No. 7,742,629 to Zarkh et al. issued on June 22,

2010, U.S. Pat. No. 7,747,047 to Okerlund et al. issued on June 29, 2010, U.S. Pat. No. 7,778,685 to Evron et al. issued on August 17, 2010, U.S. Pat. No. 7,778,686 to Vass et al. issued on August 17, 2010, U.S. Pat. No. 7,813,785 to Okerlund et al. issued on October 12, 2010, U.S. Pat. No. 7,996,063 to Vass et al. issued on August 9, 2011, U.S. Pat. No. 8,060,185 to Hunter et al. issued on November 15, 2011, and U.S. Pat. No. 8,401,616 to Verard et al. issued on March 19, 2013, each of which are incorporated herein by reference in their entireties. U.S. Pat. App. Ser. No. 13/916,353 filed June 12, 2013, and U.S. Pat. App. Ser. No. 13/707,391 filed December 6, 2012, assigned to the assignee of the present invention, the disclosures of which are incorporated by reference in its entirety herein.

Mechanical motion data, or information, may be provided to a user to assist the user in selecting a location for an implantable electrode. An exemplary graphical user interface 132 depicting mechanical motion information of a portion of a patient's heart is shown in FIG. 2. The graphical user interface 132 is configured to depict at least a portion of blood vessel anatomy 200 of a patient's heart and mechanical motion information with respect to the blood vessel anatomy 200. As shown, the blood vessel anatomy 200 is the coronary sinus located proximate the left ventricle of a patient. The blood vessel anatomy 200 further includes a plurality of branches 202 of, e.g., the coronary sinus. Each branch, as well as multiple locations within each branch, may provide candidate site regions or locations for implantable electrodes. Implantable electrodes may be implanted in locations having the latest mechanical motion time. As used herein, mechanical motion time may be the time between the onset of contraction and a common fiducial point such as e.g., onset of QRS depolarization complex for that particular cardiac cycle on an external ECG lead.

As shown, the mechanical motion time may be represented by color/grey scaling, or coding, the blood vessel anatomy 200 according to a scale 210. As shown, the scale 210 extends from dark grey/colors, which correspond to about 40 milliseconds (ms), to light white/colors, which correspond to about 240 ms. As such, a user may view the graphical user interface 132 to see, or ascertain, the

mechanical motions times of the different regions of the heart (e.g., different regions of the blood vessel anatomy). Additionally, the graphical user interface 132 may alphanumerically depict the mechanical motion times 206 for one or more regions 204 identified on blood vessel anatomy 200. Using the graphical user interface 132, a user may select a target, or candidate, location 208 for implantation that may have the latest, or near the latest, mechanical motion time. As shown, the target location 208 may have a mechanical motion time of 240 ms.

It may be desirable for target or candidate site regions or locations for implantable electrode placement to also have late electrical activation times, in addition to late mechanical motion times. The selected region, or location, such as region 208, however, may not have a late electrical activation time (e.g., indicating that the site may not be as desirable even though the mechanical motion time indicated its desirability as an implant site). As such, it is beneficial to have information about electrical activation times and mechanical motion times associated with a target or candidate site region to determine its suitability for implant.

Electrical activation data of one or more regions of a patient's heart may be determined using electrode apparatus 110 as shown in FIG. 1 and in FIGS. 3A-3B. The exemplary electrode apparatus 110 may be configured to measure body-surface potentials of a patient 14 and, more particularly, torso-surface potentials of a patient 14. As shown in FIG. 3A, the exemplary electrode apparatus 110 may include a set, or array, of electrodes 112, a strap 113, and interface/amplifier circuitry 116. The electrodes 112 may be attached, or coupled, to the strap 113 and the strap 113 may be configured to be wrapped around the torso of patient 14 such that the electrodes 112 surround the patient's heart. As further illustrated, the electrodes 112 may be positioned around the circumference of a patient 14, including the posterior, lateral, posterolateral, and anterior locations of the torso of patient 14.

Further, the electrodes 112 may be electrically connected to interface/amplifier circuitry 116 via wired connection 118. The interface/amplifier

circuitry 116 may be configured to amplify the signals from the electrodes 112 and provide the signals to the computing apparatus 140. Other exemplary systems may use a wireless connection to transmit the signals sensed by electrodes 112 to the interface/amplifier circuitry 116 and, in turn, the computing apparatus 140, e.g., as channels of data.

Although in the example of FIG. 3A the electrode apparatus 110 includes a strap 113, in other examples any of a variety of mechanisms, e.g., tape or adhesives, may be employed to aid in the spacing and placement of electrodes 112. In some examples, the strap 113 may include an elastic band, strip of tape, or cloth. In other examples, the electrodes 112 may be placed individually on the torso of a patient 14. Further, in other examples, electrodes 112 (e.g., arranged in an array) may be part of, or located within, patches, vests, and/or other means of securing the electrodes 112 to the torso of the patient 14.

The electrodes 112 may be configured to surround the heart of the patient 14 and record, or monitor, the electrical signals associated with the depolarization and repolarization of the heart after the signals have propagated through the torso of patient 14. Each of the electrodes 112 may be used in a unipolar configuration to sense the torso-surface potentials that reflect the cardiac signals. The interface/amplifier circuitry 116 may also be coupled to a return or indifferent electrode (not shown) that may be used in combination with each electrode 112 for unipolar sensing. In some examples, there may be about 12 to about 50 electrodes 112 spatially distributed around the torso of patient. Other configurations may have more or fewer electrodes 112.

The computing apparatus 140 may record and analyze the torso-surface potential signals sensed by electrodes 112 and amplified/conditioned by the interface/amplifier circuitry 116. The computing apparatus 140 may be configured to analyze the signals from the electrodes 112 to provide surrogate electrical activation data such as surrogate electrical activation times, e.g., representative of actual, or local, electrical activation times of one or more regions of the patient's heart as will be further described herein. Measurement of activation times can be

performed by picking an appropriate fiducial point (e.g., peak values, minimum values, minimum slopes, maximum slopes, zero crossings, threshold crossings, etc. of a near or far-field EGM) and measuring time between the onset of cardiac depolarization (e.g., onset of QRS complexes) and the appropriate fiducial point (e.g., within the electrical activity). The activation time between the onset of the QRS complex (or the peak Q wave) to the fiducial point may be referred to as q-LV time.

Additionally, the computing apparatus 140 may be configured to provide graphical user interfaces depicting the surrogate electrical activation times obtained using the electrode apparatus 110. Exemplary systems, methods, and/or interfaces may noninvasively use the electrical information collected using the electrode apparatus 110 to identify, select, and/or determine whether one or more regions of a patient's heart may be optimal, or desirable, for implantable electrode placement.

FIG. 3B illustrates another exemplary electrode apparatus 110 that includes a plurality of electrodes 112 configured to surround the heart of the patient 14 and record, or monitor, the electrical signals associated with the depolarization and repolarization of the heart after the signals have propagated through the torso of patient 14. The electrode apparatus 110 may include a vest 114 upon which the plurality of electrodes 112 may be attached, or to which the electrodes 112 may be coupled. In at least one embodiment, the plurality, or array, of electrodes 112 may be used to collect electrical information such as, e.g., surrogate electrical activation times. Similar to the electrode apparatus 110 of FIG. 3A, the electrode apparatus 110 of FIG. 3B may include interface/amplifier circuitry 116 electrically coupled to each of the electrodes 112 through a wired connection 118 and configured to transmit signals from the electrodes 112 to computing apparatus 140. As illustrated, the electrodes 112 may be distributed over the torso of patient 14, including, for example, the anterior, lateral, and posterior surfaces of the torso of patient 14.

The vest 114 may be formed of fabric with the electrodes 112 attached to the fabric. The vest 114 may be configured to maintain the position and spacing of electrodes 112 on the torso of the patient 14. Further, the vest 114 may be marked to assist in determining the location of the electrodes 112 on the surface of the torso of the patient 14. In some examples, there may be about 25 to about 256 electrodes 112 distributed around the torso of the patient 14, though other configurations may have more or fewer electrodes 112.

As described herein, the electrode apparatus 110 may be configured to measure electrical information (e.g., electrical signals) representing different regions of a patient's heart. More specifically, activation times of different regions of a patient's heart can be approximated from surface electrocardiogram (ECG) activation times measured using surface electrodes in proximity to surface areas corresponding to the different regions of the patient's heart.

A diagram (also referred to as body surface potential map (BSPM)) of exemplary surface locations of patient 14 mapped to regions of a patient's heart 12 to be measured using external electrode apparatus are shown in FIG. 4. Skilled artisans appreciate that a series of diagrams such as that exemplified in FIG. 4 can be displayed to a user of computing apparatus 140 while undergoing method 300. As shown, a left anterior surface location 220 may correspond to a left anterior left ventricle region 230 of the patient's heart 12, a left lateral surface location 222 may correspond to a left lateral left ventricle region 232 of the patient's heart 12, a left posterolateral surface location 224 may correspond to a posterolateral left ventricle region 234 of the patient's heart 12, and a posterior surface location 226 may correspond to a posterior left ventricle region 236 of the patient's heart 12. Thus, the electrical signals measured at the left anterior surface location 220 may be representative, or surrogates, of electrical signals of the left anterior left ventricle region 230, electrical signals measured at the left lateral surface location 222 may be representative, or surrogates, of electrical signals of the left lateral left ventricle region 232, electrical signals measured at the left posterolateral surface location 224 may be representative, or surrogates,

of electrical signals of the posterolateral left ventricle region 234, and electrical signals measured at the posterior surface location 226 may be representative, or surrogates, of electrical signals of the posterior left ventricle region 236.

Unipolar ECG data collected from electrode apparatus 110 such as, e.g., depicted in FIGS. 3A-3B, may be used to derive a sequence of ventricular activation. Information on regional, or local, ventricular activation may be inferred by looking at activation times corresponding to certain anatomic regions.

FIG. 5 depicts a method 300 for improved estimation of time of left ventricular pacing with respect to intrinsic right ventricular activation in cardiac resynchronization therapy. Method 300 serves to optimize a form of CRT referred to as fusion pacing (i.e. LV only pacing, RV only pacing). In particular, method 300 is configured to determine whether the pre-excitation interval is optimized for CRT therapy based upon evaluating the timing of delivery of left ventricular pacing in response to obtaining an objective estimate of the earliest intrinsic right ventricular activation. For the purposes of the methods described herein, pre-excitation interval is a time-interval defined by a time in which electrical stimuli is delivered to the left ventricle (LV) before a time in which an RV event is sensed. An RV event includes sensed RV pace or an intrinsic RV event.

Method 300 begins by determining a baseline rhythm. A baseline rhythm may be obtained during RV only pacing. Alternatively, the baseline rhythm is taken solely from an intrinsic rhythm of the heart. The LV is not paced when obtaining the baseline rhythm. Heart activity is sensed through one or more implanted electrodes and/or surface electrodes. A signal acquired or sensed from a single implanted electrode with respect to a distant electrode produces a unipolar electrogram (EGM) waveform while a signal acquired or sensed from a single surface electrode with respect to an indifferent electrode or composite reference like Wilson Central Terminal, produces a unipolar electrocardiogram (ECG). EGM signals and/or ECG signals are recorded during no pacing of the left ventricle (LV).

The baseline rhythm includes a variety of data. Exemplary data can include a baseline atrial event and a baseline right ventricular (RV) event sensed from an implanted medical electrical lead or a leadless device, a pre-excitation interval determined based on intrinsic rhythm parameters like duration of P-wave, intrinsic atrioventricular (A-V) timing, etc. and a plurality of activation times determined from a plurality of body-surface electrodes. Atrial events include an atrial paced or an intrinsic atrial event (i.e. depolarization) acquired from an implanted cardiac lead or a leadless device. Additionally or alternatively, the baseline rhythm includes onset of a depolarization (QRS complex) acquired through one or more a surface ECG electrodes.

The plurality of activation times are determined by the timing of a steepest negative slope on the unipolar ECG signal from each of a plurality of surface electrodes and a common fiducial point. The common fiducial point can be the onset of depolarization (Q-point) measured from a surface ECG electrode or timing of an atrial event as sensed by IMD 16. From the plurality of signals acquired from the plurality of body-surface electrodes 112, a body surface potential map (BSPM) can be generated and displayed on a graphical user interface. The user is able to review multiple BSPMs over a set period of time. BSPMs can graphically display the earliest body-surface activation time for the plurality of electrodes 112. For example, the earliest body-surface activation time can be displayed during RV only pacing at a short AV delay in a CRT patient. The image on the graphical user interface can also display the electrode from the plurality of body-surface electrodes 112 that corresponds to the earliest activation in a RV only paced rhythm.

In one or more embodiments, the earliest RV activation time is defined by an earliest activation time on right-sided electrodes among a plurality of activation times measured from a plurality of ECG electrodes 112 on the torso surface. In one or more embodiments, the earliest RV activation time is a timing of onset of a far-field RV electrogram measured from the device 16.

A determination is then made as to whether a time interval ($T_{atrial\text{-}RV}$) measured from an atrial event (T_{atria}) to a RV sense time is disparate from another time interval ($T_{atrial\ -earliest\ RVAT}$) measured from the atrial event to an earliest RV

activation time of the plurality of activation times at block 304. Disparate is defined such that the earliest RV activation time is about 40-300 ms ahead of the RV sense time as sensed by the implanted RV electrode. If the time intervals are considered disparate, another determination can be made that the RV lead is positioned in an area that is electrically late in activation. An electrically late area activates later than 40-60 ms after onset of depolarization.

In response to determining that the $T_{atrial\text{-}RV}$ is disparate from the $T_{atrial\text{-}earliest\ RVAT}$, a correction factor is then applied to the pre-excitation interval to obtain, and store into memory 82 of IMD 16 (shown in FIGs. 9A-9B), a corrected pre-excitation interval. The correction factor is based on the difference between RV sense time (i.e. RV event) and the earliest RV activation time. The preferred ranges of the correction factor can be 0-10 ms, 0-20 ms, 0-30 ms, 0-40 ms, 0-50 ms, 0-60 ms,0-70 ms, 0-80 ms, 0-90 ms, 0-100 ms, 0-110 ms, 0-120 ms, 0-130 ms, 0-140 ms, 0-150 ms. The new pre-excitation interval may be determined by a certain time delay ranging from 0 ms to 80 ms, added to the time difference between the earliest RV activation and the RV sense time if the latter two times are found to be disparate by the criteria described earlier. For example, if the value of this added delay is 20 ms, the difference between the earliest RV activation and the RV sense time happens to be 100 ms and the initially determined pre-excitation interval is 60 ms, the new pre-excitation interval after correction would be 60+(100-60) +20 ms =120 ms. In this case, the correction factor is 60 ms, meaning an additional 60 ms is added to the initially determined pre-excitation interval of 60 ms, so that the new pre-excitation interval, after correcting is 120 ms. Therefore, in this example, after correction the LV will be paced 120 ms ahead of RV sense time.

The processor 80 is then configured to signal the pulse generator to deliver electrical stimuli to a left ventricle (LV) using the corrected pre-excitation interval before RV sensing time. In one or more embodiments, delivery of LV pacing pulses is typically timed to occur 50-60 ms before RV sense time. In one or more other embodiments, delivery of LV pacing pulses is timed to occur 40-70 ms before RV sense time. While method 300 is described relative to LV only pacing, skilled artisans appreciate that fusion pacing can be applied to the RV.

Another embodiment of the present disclosure relates to method 400 depicted in FIG. 6. Blocks 402, and 406 through 408 are similar or the same as blocks 302, and 306 through 308 of FIG. 3. The description of blocks 302, and 306 through 308 of FIG. 3 are incorporated herein. Referring to block 404, an offset is determined to be present.

The offset is defined as a difference between the intrinsic rhythm activation time (T2) of an electrode from the plurality of surface electrodes 112 and an earliest time of RV activation (T1) in intrinsic rhythm (i.e. baseline rhythm). The earliest intrinsic RV activation time (T1) may be determined from activation times determined from a plurality of ECG electrodes applied on the body-surface covering the upper and/or middle areas of the anterior torso and the posterior torso. The activation times may be referenced to a common time origin like the onset of QRS complex on an ECG lead. The earliest activation time on the right anterior area of the torso would be the earliest RV activation time. The intrinsic rhythm activation time (T2) of the implanted sensing RV electrode may be determined from the near-field or far-field RV EGM recorded by the electrode, referenced to the same time-origin. The offset is equivalent to T2-T1. The offset is deemed substantially large when the offset is greater than a value which ranges from 20 ms to 50 ms. When the offset is considered substantially large, a correction factor is then applied to the pre-excitation interval to attain a corrected pre-excitation interval at block 406 for use with LV only pacing based on the offset of T2-T1. Timing of LV pacing, with respect to an RV sensing electrode based on the offset T2-T1, can result in the LV pacing being delivered. Methods 300 and 400 along with the system that implements the methods described herein improves a patient's response to CRT by accurately and reliably timing the delivery of LV pacing with respect to RV sensing.

FIG. 7 is a conceptual diagram illustrating an exemplary therapy system 10 that may be used to deliver pacing therapy to a patient 14. Patient 14 may, but not necessarily, be a human. The therapy system 10 may include an implantable medical device 16 (IMD), which may be coupled to leads 18, 20, 22. The IMD 16 may be, e.g., an implantable pacemaker, cardioverter, and/or defibrillator, that

provides electrical signals to the heart 12 of the patient 14 via electrodes coupled to one or more of the leads 18, 20, 22 (e.g., electrodes that may be implanted in accordance with the description herein, such as, with use of non-invasive selection of implantation site regions).

The leads 18, 20, 22 extend into the heart 12 of the patient 14 to sense electrical activity of the heart 12 and/or to deliver electrical stimulation to the heart 12. In the example shown in FIG. 7, the right ventricular (RV) lead 18 extends through one or more veins (not shown), the superior vena cava (not shown), and the right atrium 26, and into the right ventricle 28. The left ventricular (LV) coronary sinus lead 20 extends through one or more veins, the vena cava, the right atrium 26, and into the coronary sinus 30 to a region adjacent to the free wall of the left ventricle 32 of the heart 12. The right atrial (RA) lead 22 extends through one or more veins and the vena cava, and into the right atrium 26 of the heart 12.

The IMD 16 may sense, among other things, electrical signals attendant to the depolarization and repolarization of the heart 12 via electrodes coupled to at least one of the leads 18, 20, 22. The IMD 16 may be configured to determine or identify effective electrodes located on the leads 18, 20, 22 using the exemplary methods and processes described herein. In some examples, the IMD 16 provides pacing therapy (e.g., pacing pulses) to the heart 12 based on the electrical signals sensed within the heart 12. The IMD 16 may be operable to adjust one or more parameters associated with the pacing therapy such as, e.g., AV delay and other various timings, pulse wide, amplitude, voltage, burst length, etc. Further, the IMD 16 may be operable to use various electrode configurations to deliver pacing therapy, which may be unipolar, bipolar, quadripoloar, or further multipolar. For example, a multipolar lead may include several electrodes that can be used for delivering pacing therapy. Hence, a multipolar lead system may provide, or offer, multiple electrical vectors to pace from. A pacing vector may include at least one cathode, which may be at least one electrode located on at least one lead, and at least one anode, which may be at least one electrode

located on at least one lead (e.g., the same lead, or a different lead) and/or on the casing, or can, of the IMD. While improvement in cardiac function as a result of the pacing therapy may primarily depend on the cathode, the electrical parameters like impedance, pacing threshold voltage, current drain, longevity, etc. may be more dependent on the pacing vector, which includes both the cathode and the anode. The IMD 16 may also provide defibrillation therapy and/or cardioversion therapy via electrodes located on at least one of the leads 18, 20, 22. Further, the IMD 16 may detect arrhythmia of the heart 12, such as fibrillation of the ventricles 28, 32, and deliver defibrillation therapy to the heart 12 in the form of electrical pulses. In some examples, IMD 16 may be programmed to deliver a progression of therapies, e.g., pulses with increasing energy levels, until a fibrillation of heart 12 is stopped.

FIG. 8A-8B are conceptual diagrams illustrating the IMD 16 and the leads 18, 20, 22 of therapy system 10 of FIG. 7 in more detail. The leads 18, 20, 22 may be electrically coupled to a therapy delivery module (e.g., for delivery of pacing therapy), a sensing module (e.g., for sensing one or more signals from one or more electrodes), and/or any other modules of the IMD 16 via a connector block 34. In some examples, the proximal ends of the leads 18, 20, 22 may include electrical contacts that electrically couple to respective electrical contacts within the connector block 34 of the IMD 16. In addition, in some examples, the leads 18, 20, 22 may be mechanically coupled to the connector block 34 with the aid of set screws, connection pins, or another suitable mechanical coupling mechanism.

Each of the leads 18, 20, 22 includes an elongated insulative lead body, which may carry a number of conductors (e.g., concentric coiled conductors, straight conductors, etc.) separated from one another by insulation (e.g., tubular insulative sheaths). In the illustrated example, bipolar electrodes 40, 42 are located proximate to a distal end of the lead 18. In addition, the bipolar electrodes 44, 45, 46, 47 are located proximate to a distal end of the lead 20 and the bipolar electrodes 48, 50 are located proximate to a distal end of the lead 22.

The electrodes 40, 44, 44, 45, 46, 47, 48 may take the form of ring electrodes, and the electrodes 42, 50 may take the form of extendable helix tip electrodes mounted retractably within the insulative electrode heads 52, 54, 56, respectively. Each of the electrodes 40, 42, 44, 45, 46, 47, 48, 50 may be electrically coupled to a respective one of the conductors (e.g., coiled and/or straight) within the lead body of its associated lead 18, 20, 22, and thereby coupled to respective ones of the electrical contacts on the proximal end of the leads 18, 20, 22.

Additionally, electrodes 44, 45, 46 and 47 may have an electrode surface area of about 5.3 mm^2 to about 5.8 mm^2. Electrodes 44, 45, 46, and 47 may also be referred to as LV1, LV2, LV3, and LV4, respectively. The LV electrodes (i.e., left ventricle electrode 1 (LV1) 44, left ventricle electrode 2 (LV2) 45, left ventricle electrode 3 (LV3) 46, and left ventricle 4 (LV4) 47 etc.) on the lead 20 can be spaced apart at variable distances. For example, electrode 44 may be a distance of, e.g., about 21 millimeters (mm), away from electrode 45, electrodes 45 and 46 may be spaced a distance of, e.g. about 1.3mm to about 1.5 mm, away from each other, and electrodes 46 and 47 may be spaced a distance of, e.g. 20 mm to about 21 mm, away from each other.

The electrodes 40, 42, 44, 45, 46, 47, 48, 50 may further be used to sense electrical signals (e.g., morphological waveforms within electrograms (EGM)) attendant to the depolarization and repolarization of the heart 12. The sensed electrical signals may be used to determine which of the electrodes 40, 42, 44, 45, 46, 47, 48, 50 are the most effective in improving cardiac function. The electrical signals are conducted to the IMD 16 via the respective leads 18, 20, 22. In some examples, the IMD 16 may also deliver pacing pulses via the electrodes 40, 42, 44, 45, 46, 47, 48, 50 to cause depolarization of cardiac tissue of the patient's heart 12. In some examples, as illustrated in FIG. 8A, the IMD 16 includes one or more housing electrodes, such as housing electrode 58, which may be formed integrally with an outer surface of a housing 60 (e.g., hermetically-sealed housing) of the IMD 16 or otherwise coupled to the housing 60. Any of the electrodes 40,

42, 44, 45, 46, 47, 48 and 50 may be used for unipolar sensing or pacing in combination with housing electrode 58. In other words, any of electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58 may be used in combination to form a sensing vector, e.g., a sensing vector that may be used to evaluate and/or analyze the effectiveness of pacing therapy. It is generally understood by those skilled in the art that other electrodes can also be selected to define, or be used for, pacing and sensing vectors. Further, any of electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, which are not being used to deliver pacing therapy, may be used to sense electrical activity during pacing therapy.

As described in further detail with reference to FIG. 8A, the housing 60 may enclose a therapy delivery module that may include a stimulation generator for generating cardiac pacing pulses and defibrillation or cardioversion shocks, as well as a sensing module for monitoring the patient's heart rhythm. The leads 18, 20, 22 may also include elongated electrodes 62, 64, 66, respectively, which may take the form of a coil. The IMD 16 may deliver defibrillation shocks to the heart 12 via any combination of the elongated electrodes 62, 64, 66 and the housing electrode 58. The electrodes 58, 62, 64, 66 may also be used to deliver cardioversion pulses to the heart 12. Further, the electrodes 62, 64, 66 may be fabricated from any suitable electrically conductive material, such as, but not limited to, platinum, platinum alloy, and/or other materials known to be usable in implantable defibrillation electrodes. Since electrodes 62, 64, 66 are not generally configured to deliver pacing therapy, any of electrodes 62, 64, 66 may be used to sense electrical activity (e.g., for use in determining electrode effectiveness, for use in analyzing pacing therapy effectiveness, etc.) and may be used in combination with any of electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58. In at least one embodiment, the RV elongated electrode 62 may be used to sense electrical activity of a patient's heart during the delivery of pacing therapy (e.g., in combination with the housing electrode 58 forming a RV elongated coil, or defibrillation electrode-to-housing electrode vector).

The configuration of the exemplary therapy system 10 illustrated in FIGS. 7-9 is merely one example. In other examples, the therapy system may include epicardial leads and/or patch electrodes instead of or in addition to the transvenous leads 18, 20, 22 illustrated in FIG. 7. Further, in one or more embodiments, the IMD 16 need not be implanted within the patient 14. For example, the IMD 16 may deliver various cardiac therapies to the heart 12 via percutaneous leads that extend through the skin of the patient 14 to a variety of positions within or outside of the heart 12. In one or more embodiments, the system 10 may utilize wireless pacing (e.g., using energy transmission to the intracardiac pacing component(s) via ultrasound, inductive coupling, RF, etc.) and sensing cardiac activation using electrodes on the can/housing and/or on subcutaneous leads.

In other examples of therapy systems that provide electrical stimulation therapy to the heart 12, such therapy systems may include any suitable number of leads coupled to the IMD 16, and each of the leads may extend to any location within or proximate to the heart 12. For example, other examples of therapy systems may include three transvenous leads located as illustrated in FIGS. 15-17. Still further, other therapy systems may include a single lead that extends from the IMD 16 into the right atrium 26 or the right ventricle 28, or two leads that extend into a respective one of the right atrium 26 and the right ventricle 28.

FIG. 9A is a functional block diagram of one exemplary configuration of the IMD 16. As shown, the IMD 16 may include a control module 81, a therapy delivery module 84 (e.g., which may include a stimulation generator), a sensing module 86, and a power source 90.

The control module 81 may include a processor 80, memory 82, and a telemetry module 88. The memory 82 may include computer-readable instructions that, when executed, e.g., by the processor 80, cause the IMD 16 and/or the control module 81 to perform various functions attributed to the IMD 16 and/or the control module 81 described herein. Further, the memory 82 may include any volatile, non-volatile, magnetic, optical, and/or electrical media, such

as a random access memory (RAM), read-only memory (ROM), non-volatile RAM (NVRAM), electrically-erasable programmable ROM (EEPROM), flash memory, and/or any other digital media. An exemplary capture management module may be the left ventricular capture management (LVCM) module described in U.S. Pat. No. 7,684,863 entitled "LV THRESHOLD MEASUREMENT AND CAPTURE MANAGEMENT" and issued March 23, 2010, which is incorporated herein by reference in its entirety.

The processor 80 of the control module 81 may include any one or more of a microprocessor, a controller, a digital signal processor (DSP), an application specific integrated circuit (ASIC), a field-programmable gate array (FPGA), and/or equivalent discrete or integrated logic circuitry. In some examples, the processor 80 may include multiple components, such as any combination of one or more microprocessors, one or more controllers, one or more DSPs, one or more ASICs, and/or one or more FPGAs, as well as other discrete or integrated logic circuitry. The functions attributed to the processor 80 herein may be embodied as software, firmware, hardware, or any combination thereof.

The control module 81 may be used to determine the effectiveness of the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66 using the exemplary methods and/or processes described herein according to a selected one or more programs, which may be stored in the memory 82. Further, the control module 81 may control the therapy delivery module 84 to deliver therapy (e.g., electrical stimulation therapy such as pacing) to the heart 12 according to a selected one or more therapy programs, which may be stored in the memory 82. More, specifically, the control module 81 (e.g., the processor 80) may control various parameters of the electrical stimulus delivered by the therapy delivery module 84 such as, e.g., AV delays, pacing pulses with the amplitudes, pulse widths, frequency, or electrode polarities, etc., which may be specified by one or more selected therapy programs (e.g., AV delay adjustment programs, pacing therapy programs, pacing recovery programs, capture management programs, etc.). As shown, the therapy delivery module 84 is electrically coupled to electrodes 40, 42,

44, 45, 46, 47, 48, 50, 58, 62, 64, 66, e.g., via conductors of the respective lead 18, 20, 22, or, in the case of housing electrode 58, via an electrical conductor disposed within housing 60 of IMD 16. Therapy delivery module 84 may be configured to generate and deliver electrical stimulation therapy such as pacing therapy to the heart 12 using one or more of the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66.

For example, therapy delivery module 84 may deliver pacing stimulus (e.g., pacing pulses) via ring electrodes 40, 44, 45, 46, 47, 48 coupled to leads 18, 20, and 22, respectively, and/or helical tip electrodes 42 and 50 of leads 18 and 22. Further, for example, therapy delivery module 84 may deliver defibrillation shocks to heart 12 via at least two of electrodes 58, 62, 64, 66. In some examples, therapy delivery module 84 may be configured to deliver pacing, cardioversion, or defibrillation stimulation in the form of electrical pulses. In other examples, therapy delivery module 84 may be configured deliver one or more of these types of stimulation in the form of other signals, such as sine waves, square waves, and/or other substantially continuous time signals.

The IMD 16 may further include a switch module 85 and the control module 81 (e.g., the processor 80) may use the switch module 85 to select, e.g., via a data/address bus, which of the available electrodes are used to deliver therapy such as pacing pulses for pacing therapy, or which of the available electrodes are used for sensing. The switch module 85 may include a switch array, switch matrix, multiplexer, or any other type of switching device suitable to selectively couple the sensing module 86 and/or the therapy delivery module 84 to one or more selected electrodes. More specifically, the therapy delivery module 84 may include a plurality of pacing output circuits. Each pacing output circuit of the plurality of pacing output circuits may be selectively coupled, e.g., using the switch module 85, to one or more of the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66 (e.g., a pair of electrodes for delivery of therapy to a pacing vector). In other words, each electrode can be selectively coupled to one of the pacing output circuits of the therapy delivery module using the switching module 85.

The sensing module 86 is coupled (e.g., electrically coupled) to sensing apparatus, which may include, among additional sensing apparatus, the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66 to monitor electrical activity of the heart 12, e.g., electrocardiogram (ECG)/electrogram (EGM) signals, etc. The ECG/EGM signals may be used to measure or monitor activation times (e.g., ventricular activations times, etc.), heart rate (HR), heart rate variability (HRV), heart rate turbulence (HRT), deceleration/acceleration capacity, deceleration sequence incidence, T-wave alternans (TWA), P-wave to P-wave intervals (also referred to as the P-P intervals or A-A intervals), R-wave to R-wave intervals (also referred to as the R-R intervals or V-V intervals), P-wave to QRS complex intervals (also referred to as the P-R intervals, A-V intervals, or P-Q intervals), QRS-complex morphology, ST segment (i.e., the segment that connects the QRS complex and the T-wave), T-wave changes, QT intervals, electrical vectors, etc.

The switch module 85 may be also be used with the sensing module 86 to select which of the available electrodes are used, or enabled, to, e.g., sense electrical activity of the patient's heart (e.g., one or more electrical vectors of the patient's heart using any combination of the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66). Likewise, the switch module 85 may be also be used with the sensing module 86 to select which of the available electrodes are not to be used (e.g., disabled) to, e.g., sense electrical activity of the patient's heart (e.g., one or more electrical vectors of the patient's heart using any combination of the electrodes 40, 42, 44, 45, 46, 47, 48, 50, 58, 62, 64, 66), etc. In some examples, the control module 81 may select the electrodes that function as sensing electrodes via the switch module within the sensing module 86, e.g., by providing signals via a data/address bus.

In some examples, sensing module 86 includes a channel that includes an amplifier with a relatively wider pass band than the R-wave or P-wave amplifiers. Signals from the selected sensing electrodes may be provided to a multiplexer, and thereafter converted to multi-bit digital signals by an analog-to-digital

converter for storage in memory 82, e.g., as an electrogram (EGM). In some examples, the storage of such EGMs in memory 82 may be under the control of a direct memory access circuit.

In some examples, the control module 81 may operate as an interrupt driven device, and may be responsive to interrupts from pacer timing and control module, where the interrupts may correspond to the occurrences of sensed P-waves and R-waves and the generation of cardiac pacing pulses. Any necessary mathematical calculations may be performed by the processor 80 and any updating of the values or intervals controlled by the pacer timing and control module may take place following such interrupts. A portion of memory 82 may be configured as a plurality of recirculating buffers, capable of holding one or more series of measured intervals, which may be analyzed by, e.g., the processor 80 in response to the occurrence of a pace or sense interrupt to determine whether the patient's heart 12 is presently exhibiting atrial or ventricular tachyarrhythmia.

The telemetry module 88 of the control module 81 may include any suitable hardware, firmware, software, or any combination thereof for communicating with another device, a programmer, such as that which is described in Medtronic Vitatron Reference Manual CARELINK ENCORE™ (2013) available at http://manuals.medtronic.com/manuals/main/as/en/manual, incorporated by reference in its entirety. For example, under the control of the processor 80, the telemetry module 88 may receive downlink telemetry from and send uplink telemetry to a programmer with the aid of an antenna, which may be internal and/or external. The processor 80 may provide the data to be uplinked to a programmer and the control signals for the telemetry circuit within the telemetry module 88, e.g., via an address/data bus. In some examples, the telemetry module 88 may provide received data to the processor 80 via a multiplexer.

The various components of the IMD 16 are further coupled to a power source 90, which may include a rechargeable or non-rechargeable battery. A non-rechargeable battery may be selected to last for several years, while a

rechargeable battery may be inductively charged from an external device, e.g., on a daily or weekly basis.

FIG. 9B is another embodiment of a functional block diagram for IMD 16. FIG. 17B depicts bipolar RA lead 22, bipolar RV lead 18, and bipolar LV CS lead 20 without the LA CS pace/sense electrodes and coupled with an implantable pulse generator (IPG) circuit 31 having programmable modes and parameters of a bi-ventricular DDD/R type known in the pacing art. In turn, the sensor signal processing circuit 91 indirectly couples to the timing circuit 83 and via data and control bus to microcomputer circuitry 33. The IPG circuit 31 is illustrated in a functional block diagram divided generally into a microcomputer circuit 33 and a pacing circuit 21. The pacing circuit 21 includes the digital controller/timer circuit 83, the output amplifiers circuit 51, the sense amplifiers circuit 55, the RF telemetry transceiver 41, the activity sensor circuit 35 as well as a number of other circuits and components described below.

Crystal oscillator circuit 89 provides the basic timing clock for the pacing circuit 21, while battery 29 provides power. Power-on-reset circuit 87 responds to initial connection of the circuit to the battery for defining an initial operating condition and similarly, resets the operative state of the device in response to detection of a low battery condition. Reference mode circuit 37 generates stable voltage reference and currents for the analog circuits within the pacing circuit 21, while analog to digital converter ADC and multiplexer circuit 39 digitizes analog signals and voltage to provide real time telemetry if a cardiac signals from sense amplifiers 55, for uplink transmission via RF transmitter and receiver circuit 41. Voltage reference and bias circuit 37, ADC and multiplexer 39, power-on-reset circuit 87 and crystal oscillator circuit 89 may correspond to any of those presently used in current marketed implantable cardiac pacemakers.

If the IPG is programmed to a rate responsive mode, the signals output by one or more physiologic sensor are employed as a rate control parameter (RCP) to derive a physiologic escape interval. For example, the escape interval is adjusted proportionally to the patient's activity level developed in the patient

activity sensor (PAS) circuit 35 in the depicted, exemplary IPG circuit 31. The patient activity sensor 27 is coupled to the IPG housing and may take the form of a piezoelectric crystal transducer as is well known in the art and its output signal is processed and used as the RCP. Sensor 27 generates electrical signals in response to sensed physical activity that are processed by activity circuit 35 and provided to digital controller/timer circuit 83. Activity circuit 35 and associated sensor 27 may correspond to the circuitry disclosed in U.S. Pat. No. 5,052,388 entitled "METHOD AND APPARATUS FOR IMPLEMENTING ACTIVITY SENSING IN A PULSE GENERATOR" and issued on October 1, 1991 and U.S. Pat. No. 4,428,378 entitled "RATE ADAPTIVE PACER" and issued on January 31, 1984, each of which are incorporated herein by reference in their entireties. Similarly, the exemplary systems, apparatus, and methods described herein may be practiced in conjunction with alternate types of sensors such as oxygenation sensors, pressure sensors, pH sensors and respiration sensors, all well known for use in providing rate responsive pacing capabilities. Alternately, QT time may be used as the rate indicating parameter, in which case no extra sensor is required. Similarly, the exemplary embodiments described herein may also be practiced in non-rate responsive pacemakers.

Data transmission to and from the external programmer is accomplished by way of the telemetry antenna 57 and an associated RF transceiver 41, which serves both to demodulate received downlink telemetry and to transmit uplink telemetry. Uplink telemetry capabilities will typically include the ability to transmit stored digital information, e.g. operating modes and parameters, EGM histograms, and other events, as well as real time EGMs of atrial and/or ventricular electrical activity and marker channel pulses indicating the occurrence of sensed and paced depolarizations in the atrium and ventricle, as are well known in the pacing art.

Microcomputer 33 contains a microprocessor 80 and associated system clock and on-processor RAM and ROM chips 82A and 82B, respectively. In addition, microcomputer circuit 33 includes a separate RAM/ROM chip 82C to provide additional memory capacity. Microprocessor 80 normally operates in a

reduced power consumption mode and is interrupt driven. Microprocessor 80 is awakened in response to defined interrupt events, which may include A-TRIG, RV-TRIG, LV-TRIG signals generated by timers in digital timer/controller circuit 83 and A-EVENT, RV-EVENT, and LV-EVENT signals generated by sense amplifiers circuit 55, among others. The specific values of the intervals and delays timed out by digital controller/timer circuit 83 are controlled by the microcomputer circuit 33 by way of data and control bus from programmed-in parameter values and operating modes. In addition, if programmed to operate as a rate responsive pacemaker, a timed interrupt, e.g., every cycle or every two seconds, may be provided in order to allow the microprocessor to analyze the activity sensor data and update the basic A-A, V-A, or V-V escape interval, as applicable. In addition, the microprocessor 80 may also serve to define variable, operative AV delay intervals and the energy delivered to each ventricle.

In one embodiment, microprocessor 80 is a custom microprocessor adapted to fetch and execute instructions stored in RAM/ROM unit 82 in a conventional manner. It is contemplated, however, that other implementations may be suitable to practice the present invention. For example, an off-the-shelf, commercially available microprocessor or microcontroller, or custom application-specific, hardwired logic, or state-machine type circuit may perform the functions of microprocessor 80.

Digital controller/timer circuit 83 operates under the general control of the microcomputer 33 to control timing and other functions within the pacing circuit 320 and includes a set of timing and associated logic circuits of which certain ones pertinent to the present invention are depicted. The depicted timing circuits include URI/LRI timers 83A, V-V delay timer 83B, intrinsic interval timers 83C for timing elapsed V-EVENT to V-EVENT intervals or V-EVENT to A-EVENT intervals or the V-V conduction interval, escape interval timers 83D for timing A-A, V-A, and/or V-V pacing escape intervals, an AV delay interval timer 83E for timing the A-LVp delay (or A-RVp delay) from a preceding A-EVENT or A-TRIG, a post-

ventricular timer 83F for timing post-ventricular time periods, and a date/time clock 83G.

The AV delay interval timer 83E is loaded with an appropriate delay interval for one ventricular chamber (e.g., either an A-RVp delay or an A-LVp delay as determined using known methods) to time-out starting from a preceding A-PACE or A-EVENT. The interval timer 83E triggers pacing stimulus delivery, and can be based on one or more prior cardiac cycles (or from a data set empirically derived for a given patient).

The post-event timer 83F time out the post-ventricular time period following an RV-EVENT or LV-EVENT or a RV-TRIG or LV-TRIG and post-atrial time periods following an A-EVENT or A-TRIG. The durations of the post-event time periods may also be selected as programmable parameters stored in the microcomputer 33. The post-ventricular time periods include the PVARP, a post-atrial ventricular blanking period (PAVBP), a ventricular blanking period (VBP), a post-ventricular atrial blanking period (PVARP) and a ventricular refractory period (VRP) although other periods can be suitably defined depending, at least in part, on the operative circuitry employed in the pacing engine. The post-atrial time periods include an atrial refractory period (ARP) during which an A-EVENT is ignored for the purpose of resetting any AV delay, and an atrial blanking period (ABP) during which atrial sensing is disabled. It should be noted that the starting of the post-atrial time periods and the AV delays can be commenced substantially simultaneously with the start or end of each A-EVENT or A-TRIG or, in the latter case, upon the end of the A-PACE which may follow the A-TRIG. Similarly, the starting of the post-ventricular time periods and the V-A escape interval can be commenced substantially simultaneously with the start or end of the V-EVENT or V-TRIG or, in the latter case, upon the end of the V-PACE which may follow the V-TRIG. The microprocessor 80 also optionally calculates AV delays, post-ventricular time periods, and post-atrial time periods that vary with the sensor based escape interval established in response to the RCP(s) and/or with the intrinsic atrial rate.

The output amplifiers circuit 51 contains a RA pace pulse generator (and a LA pace pulse generator if LA pacing is provided), a RV pace pulse generator, and a LV pace pulse generator or corresponding to any of those presently employed in commercially marketed cardiac pacemakers providing atrial and ventricular pacing. In order to trigger generation of an RV-PACE or LV-PACE pulse, digital controller/timer circuit 83 generates the RV-TRIG signal at the time-out of the A-RVp delay (in the case of RV pre-excitation) or the LV-TRIG at the time-out of the A-LVp delay (in the case of LV pre-excitation) provided by AV delay interval timer 83E (or the V-V delay timer 83B). Similarly, digital controller/timer circuit 83 generates an RA-TRIG signal that triggers output of an RA-PACE pulse (or an LA-TRIG signal that triggers output of an LA-PACE pulse, if provided) at the end of the V-A escape interval timed by escape interval timers 83D.

The output amplifiers circuit 51 includes switching circuits for coupling selected pace electrode pairs from among the lead conductors and the IND_CAN electrode 20 to the RA pace pulse generator (and LA pace pulse generator if provided), RV pace pulse generator and LV pace pulse generator. Pace/sense electrode pair selection and control circuit 53 selects lead conductors and associated pace electrode pairs to be coupled with the atrial and ventricular output amplifiers within output amplifiers circuit 51 for accomplishing RA, LA, RV and LV pacing.

The sense amplifiers circuit 55 contains sense amplifiers corresponding to any of those presently employed in contemporary cardiac pacemakers for atrial and ventricular pacing and sensing. High impedance P-wave and R-wave sense amplifiers may be used to amplify a voltage difference signal that is generated across the sense electrode pairs by the passage of cardiac depolarization wavefronts. The high impedance sense amplifiers use high gain to amplify the low amplitude signals and rely on pass band filters, time domain filtering and amplitude threshold comparison to discriminate a P-wave or R-wave from

background electrical noise. Digital controller/timer circuit 83 controls sensitivity settings of the atrial and ventricular sense amplifiers 55.

The sense amplifiers are typically uncoupled from the sense electrodes during the blanking periods before, during, and after delivery of a pace pulse to any of the pace electrodes of the pacing system to avoid saturation of the sense amplifiers. The sense amplifiers circuit 55 includes blanking circuits for uncoupling the selected pairs of the lead conductors and the IND-CAN electrode 20 from the inputs of the RA sense amplifier (and LA sense amplifier if provided), RV sense amplifier and LV sense amplifier during the ABP, PVABP and VBP. The sense amplifiers circuit 55 also includes switching circuits for coupling selected sense electrode lead conductors and the IND-CAN electrode 20 to the RA sense amplifier (and LA sense amplifier if provided), RV sense amplifier and LV sense amplifier. Again, sense electrode selection and control circuit 53 selects conductors and associated sense electrode pairs to be coupled with the atrial and ventricular sense amplifiers within the output amplifiers circuit 51 and sense amplifiers circuit 55 for accomplishing RA, LA, RV and LV sensing along desired unipolar and bipolar sensing vectors.

Right atrial depolarizations or P-waves in the RA-SENSE signal that are sensed by the RA sense amplifier result in a RA-EVENT signal that is communicated to the digital controller/timer circuit 83. Similarly, left atrial depolarizations or P-waves in the LA-SENSE signal that are sensed by the LA sense amplifier, if provided, result in a LA-EVENT signal that is communicated to the digital controller/timer circuit 83. Ventricular depolarizations or R-waves in the RV-SENSE signal are sensed by a ventricular sense amplifier result in an RV-EVENT signal that is communicated to the digital controller/timer circuit 83. Similarly, ventricular depolarizations or R-waves in the LV-SENSE signal are sensed by a ventricular sense amplifier result in an LV-EVENT signal that is communicated to the digital controller/timer circuit 83. The RV-EVENT, LV-EVENT, and RA-EVENT, LA-SENSE signals may be refractory or non-refractory,

and can inadvertently be triggered by electrical noise signals or aberrantly conducted depolarization waves rather than true R-waves or P-waves.

The techniques described in this disclosure, including those attributed to the IMD 16, the computing apparatus 140, and/or various constituent components, may be implemented, at least in part, in hardware, software, firmware, or any combination thereof. For example, various aspects of the techniques may be implemented within one or more processors, including one or more microprocessors, DSPs, ASICs, FPGAs, or any other equivalent integrated or discrete logic circuitry, as well as any combinations of such components, embodied in programmers, such as physician or patient programmers, stimulators, image processing devices, or other devices. The term "module," "processor," or "processing circuitry" may generally refer to any of the foregoing logic circuitry, alone or in combination with other logic circuitry, or any other equivalent circuitry.

Such hardware, software, and/or firmware may be implemented within the same device or within separate devices to support the various operations and functions described in this disclosure. In addition, any of the described units, modules, or components may be implemented together or separately as discrete but interoperable logic devices. Depiction of different features as modules or units is intended to highlight different functional aspects and does not necessarily imply that such modules or units must be realized by separate hardware or software components. Rather, functionality associated with one or more modules or units may be performed by separate hardware or software components, or integrated within common or separate hardware or software components.

When implemented in software, the functionality ascribed to the systems, devices and techniques described in this disclosure may be embodied as instructions on a computer-readable medium such as RAM, ROM, NVRAM, EEPROM, FLASH memory, magnetic data storage media, optical data storage media, or the like. The instructions may be executed by one or more processors to support one or more aspects of the functionality described in this disclosure.

Skilled artisans will appreciate that the methods described herein can being implemented during implant of a medical device and post-implant such as at a follow-up visit to ensure the IMD 16 is properly functioning. Additionally, the methods described herein can be implemented while the patient is at rest (e.g. sleeping). This disclosure has been provided with reference to illustrative embodiments and is not meant to be construed in a limiting sense. As described previously, one skilled in the art will recognize that other various illustrative applications may use the techniques as described herein to take advantage of the beneficial characteristics of the apparatus and methods described herein. Various modifications of the illustrative embodiments, as well as additional embodiments of the disclosure, will be apparent upon reference to this description.

What is claimed:

1. A system of cardiac pacing comprising:

a) determining a baseline rhythm, the baseline rhythm includes a baseline atrial event and a baseline right ventricular (RV) event from an implanted cardiac lead or a leadless device, a pre-excitation interval determined from the baseline atrial event and the baseline RV event, and a plurality of activation times determined from the plurality of body-surface electrodes;

b) determining an offset, the offset defined as difference between the intrinsic rhythm activation time (T2) of an electrode (T2) an earliest time of RV activation (T1) in intrinsic rhythm; and

c) applying a correction factor to the pre-excitation interval for left ventricle (LV) only pacing based on the offset T2-T1; and

d) configuring the processor to signal the pulse generator to deliver electrical stimuli to a LV using the corrected pre-excitation interval before the RV sensing time.

2. The system of claim 1 further comprising:

determining an offset, the offset defined as activation time of an electrode (T2) – an earliest time of activation (T1); and

setting a timing of LV pacing with respect to an RV sensing electrode based on the offset T2-T1.

3. The system of any of claims 1-2 further comprising:

determining whether the offset is a substantially large offset.

4. The system of any of claims 1-3 further comprising:

delivering LV pacing substantially earlier than RV sense in response to determining the offset is substantially large.

5. The system of any of claims 1-4 wherein the offset is substantially larger provided the offset is greater than a value which ranges from 20 ms to 50 ms.

6. The system of any of claims 1-5 wherein each of the plurality of activation times are determined by a timing of a steepest negative slope on the unipolar ECG signal from each of a plurality of surface electrodes and a common fiducial point.

7. The system of claim 6 wherein the common fiducial point is the onset of depolarization (Q-point) measured from a surface ECG electrode or timing of an atrial event as sensed by an implantable medical device.

8. The system of any of claims 1-6 wherein the correction factor to the pre-excitation interval is in response to determining a time interval ($T_{atrial\text{-}RV}$) measured from an atrial event to a RV sense time is disparate from another time interval ($T_{atrial\text{ - earliest RVAT}}$).

9. The system of any of claims 1-8 wherein T2 is time interval $T_{atrial\text{-}RV}$.

10. The system of any of claims 1-9 wherein T1 is $T_{atrial\text{-earliest RV activation time}}$ (RVAT).

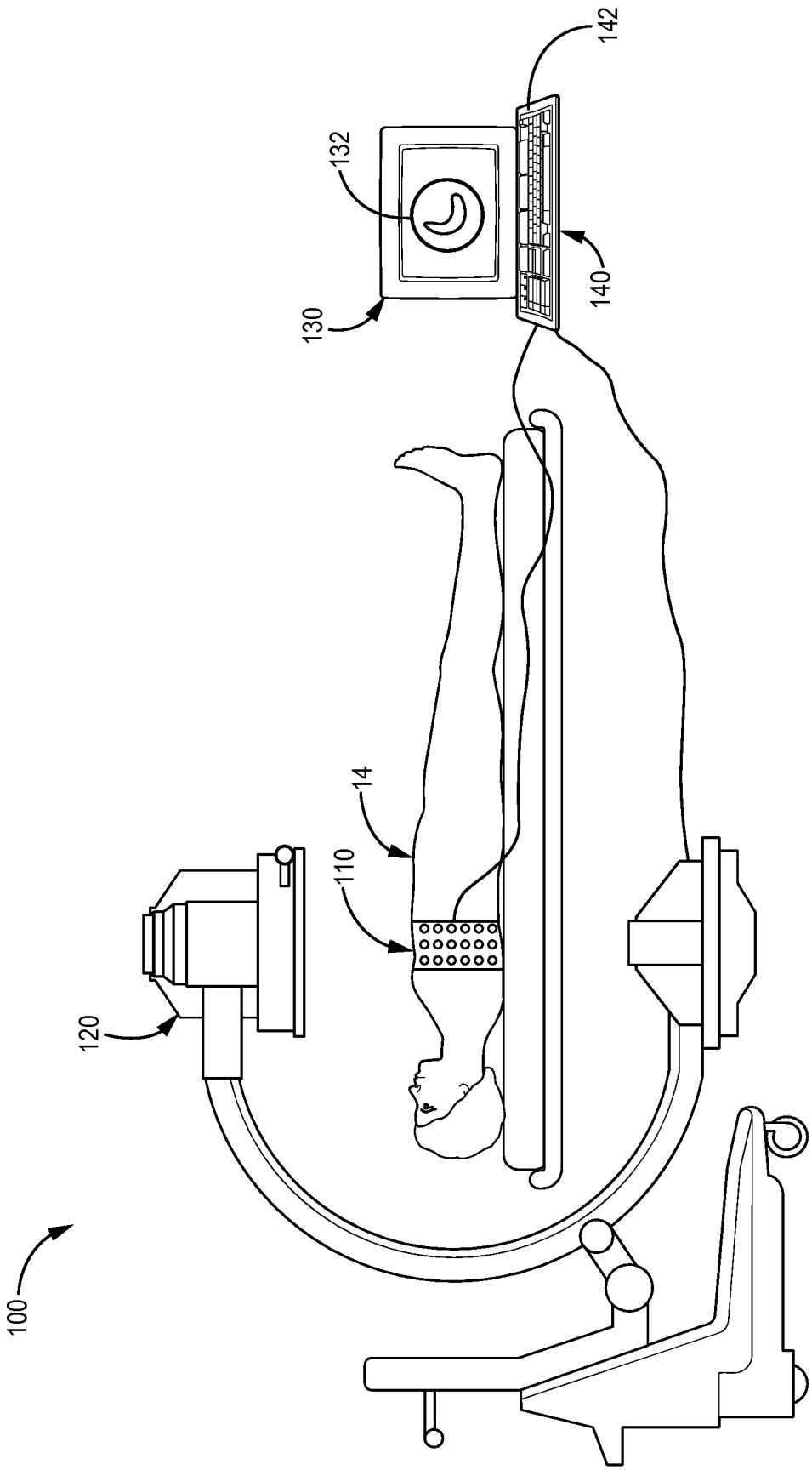


Fig. 1

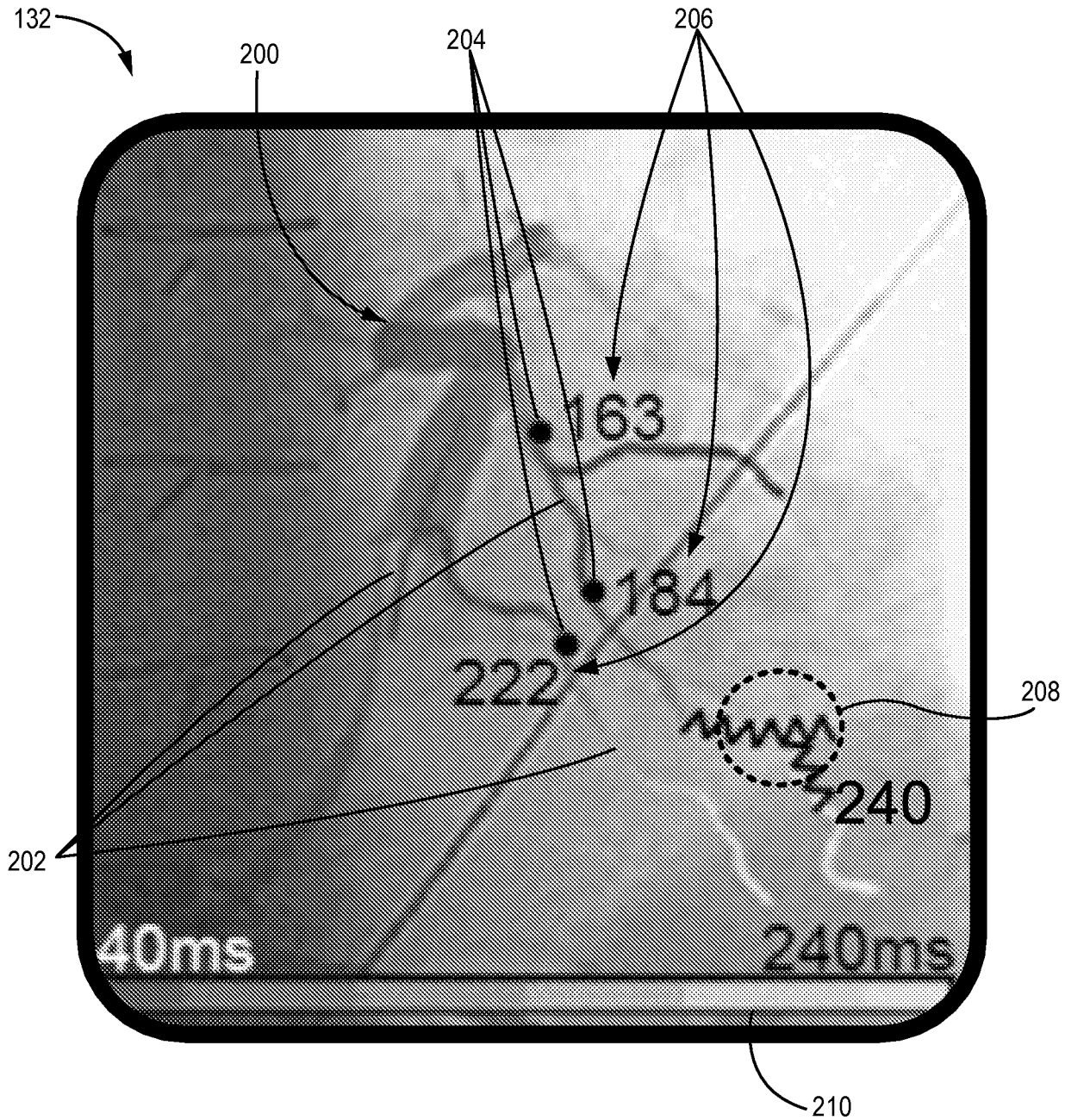
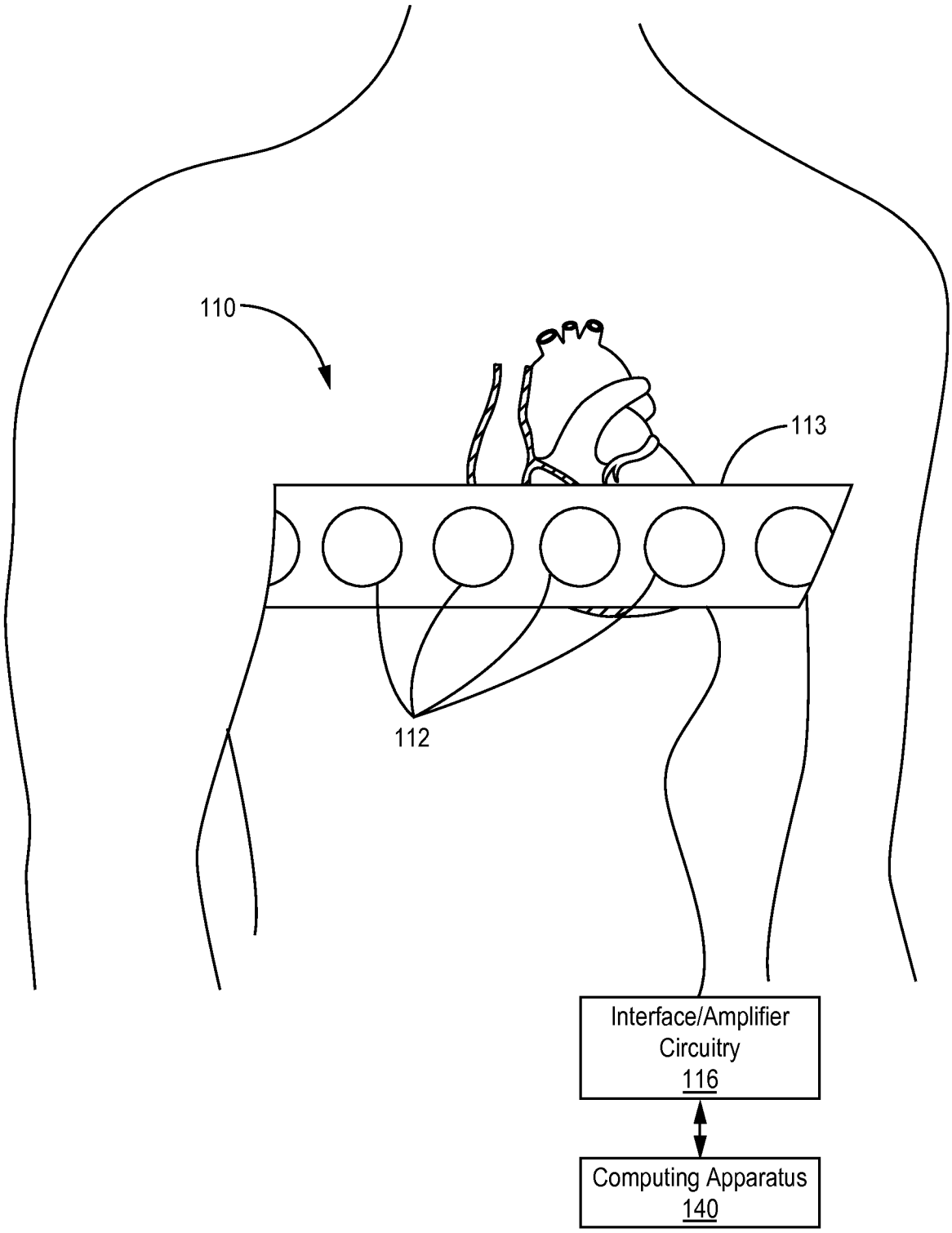


Fig. 2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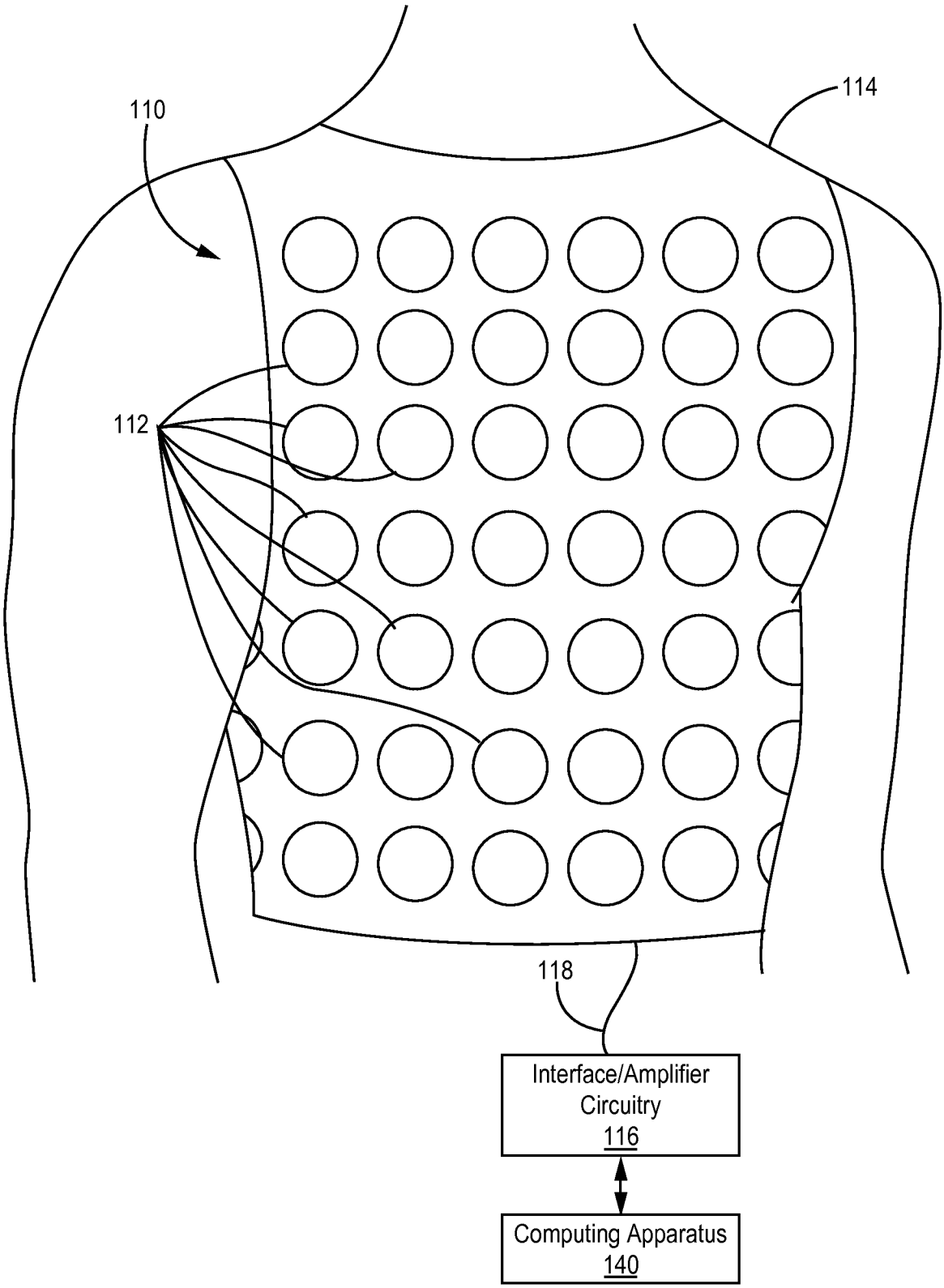
Interface/Amplifier Circuitry
116
Computing Apparatus
140

Fig. 3A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Interface/Amplifier Circuitry
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Computing Apparatus
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Fig. 3B

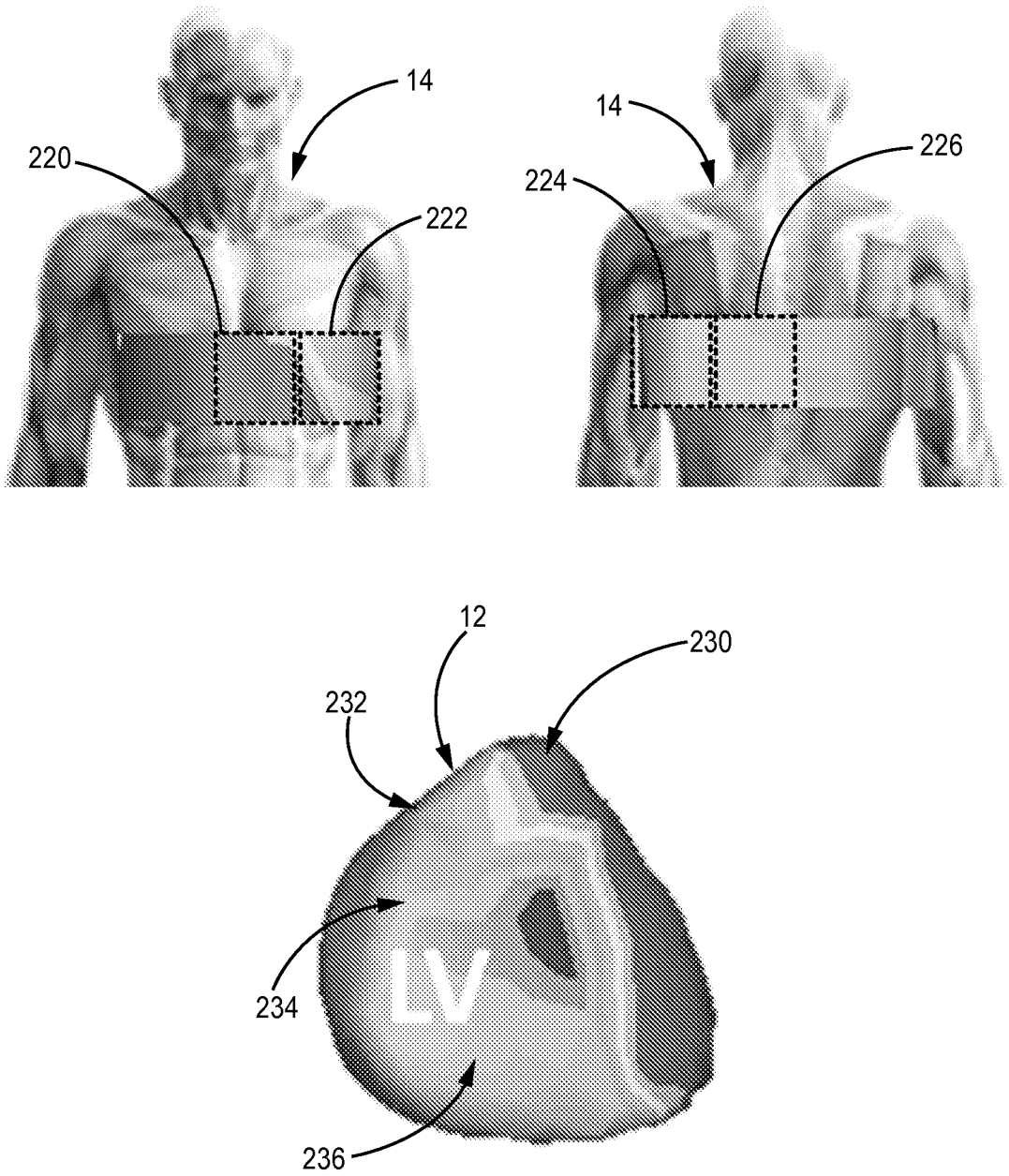

Fig. 4

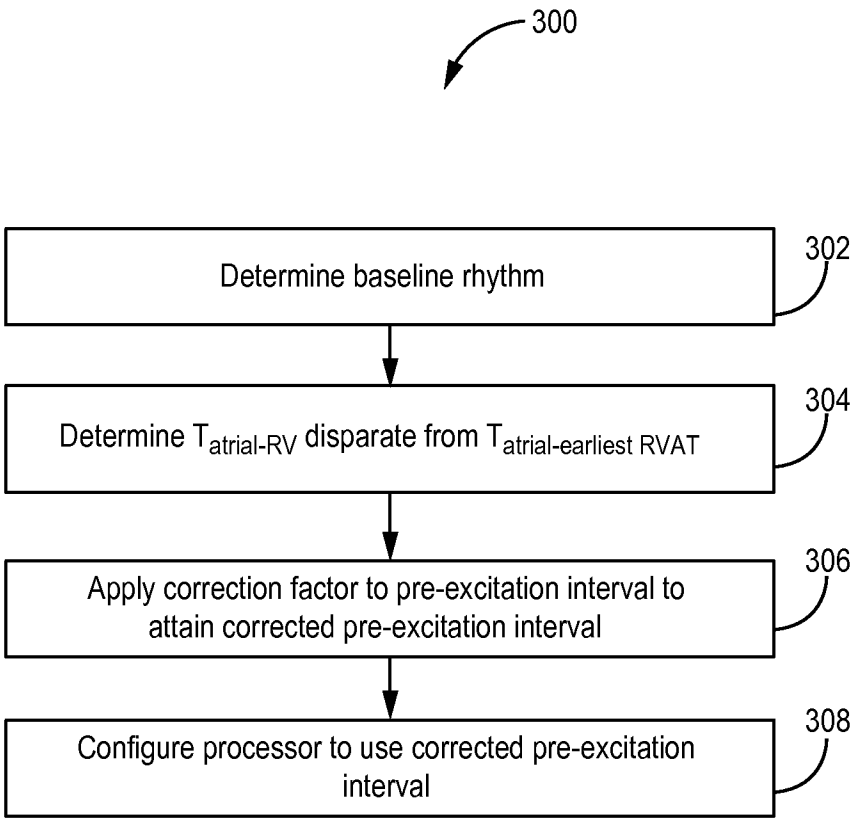
300
Determine baseline rhythm
302
Determine $T_{atrial-RV}$ disparate from $T_{atrial-earliest\ RVAT}$
304
Apply correction factor to pre-excitation interval to attain corrected pre-excitation interval
306
Configure processor to use corrected pre-excitation interval
308

Fig. 5

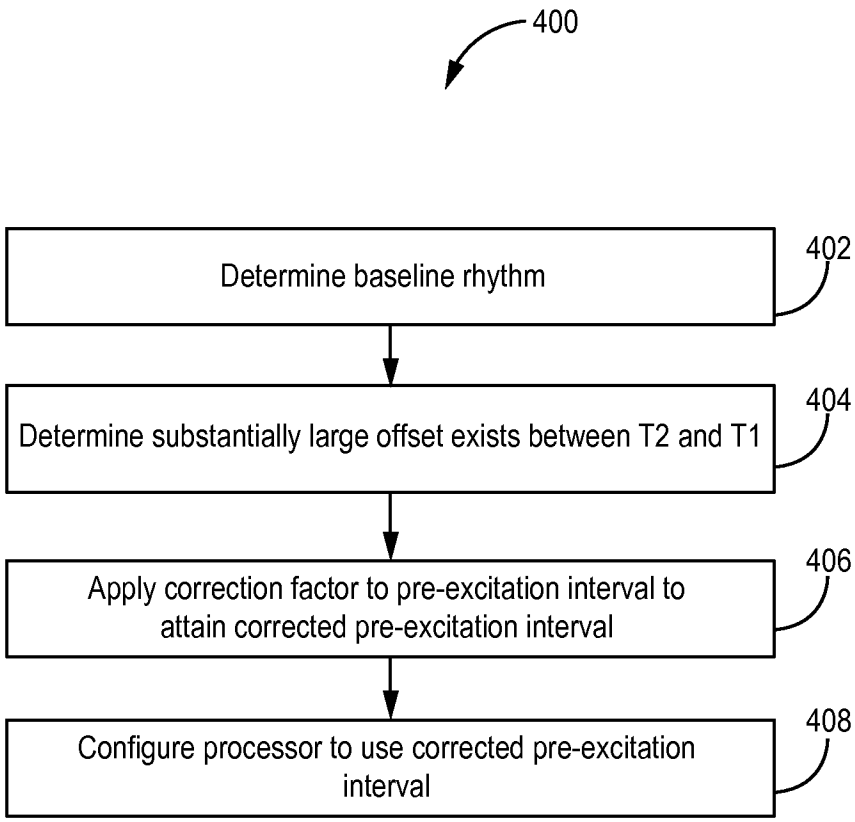
400
Determine baseline rhythm
402
Determine substantially large offset exists between T2 and T1
404
Apply correction factor to pre-excitation interval to attain corrected pre-excitation interval
406
Configure processor to use corrected pre-excitation interval
408

Fig. 6

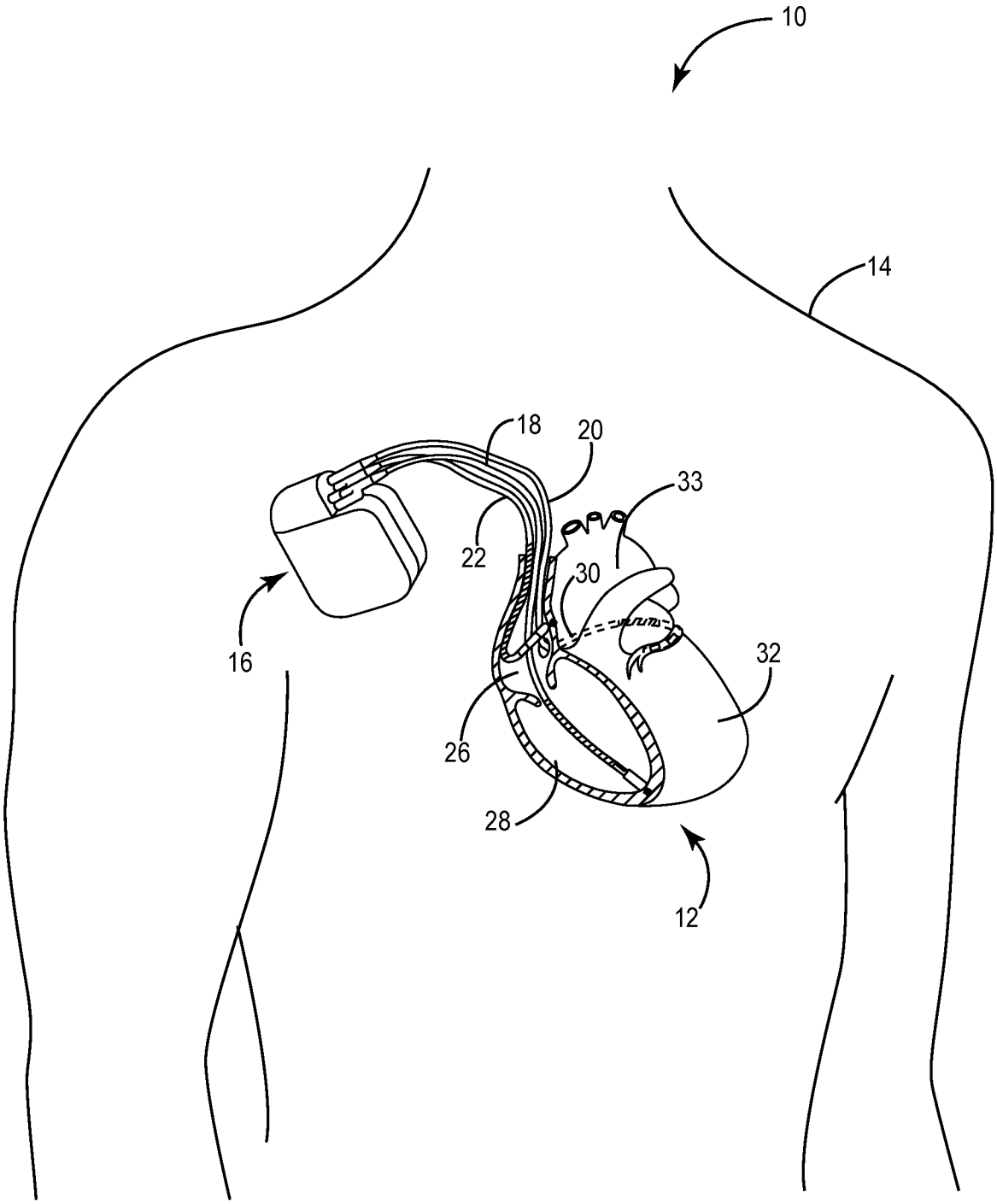

Fig. 7

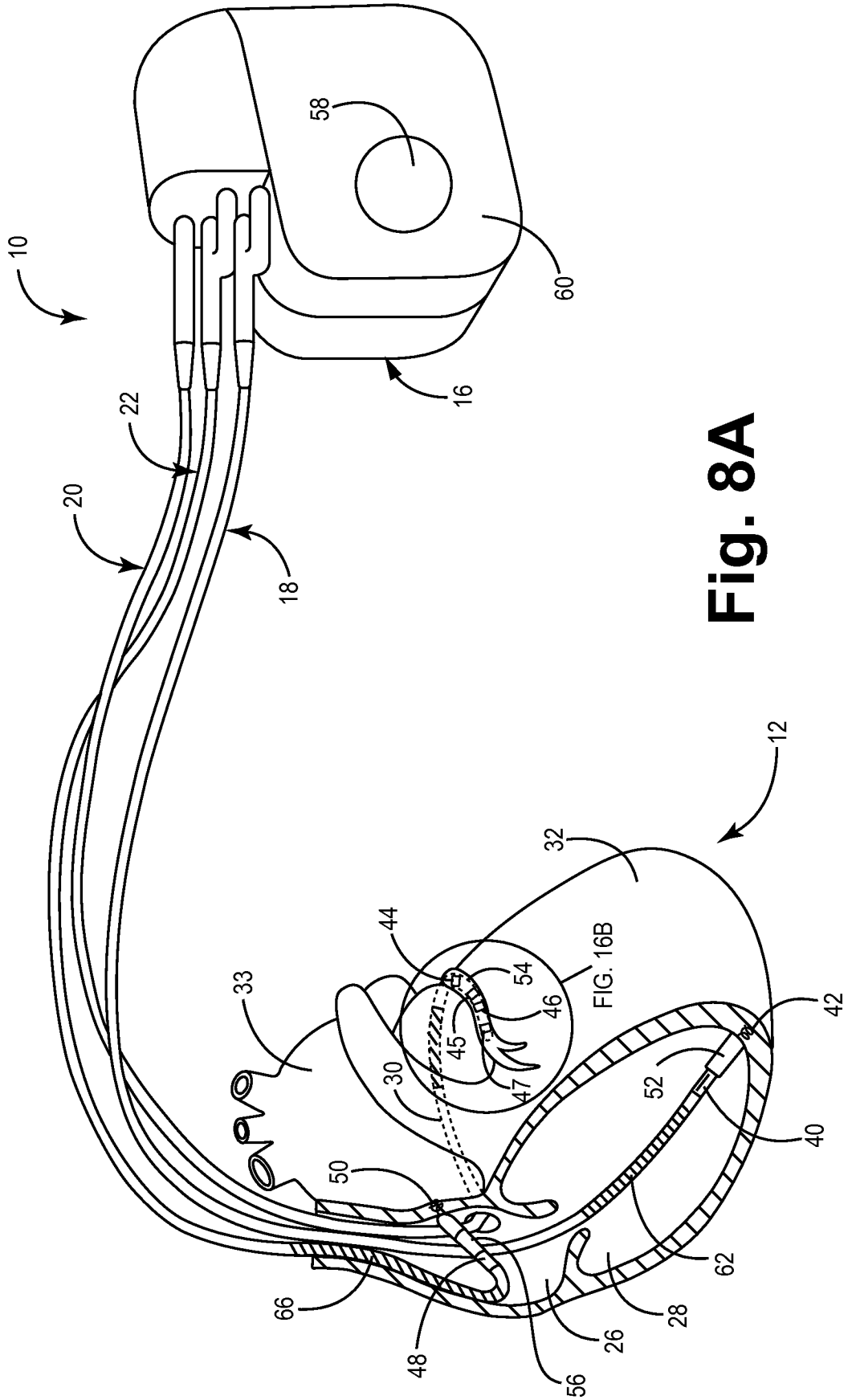
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FIG. 16B
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Fig. 8A

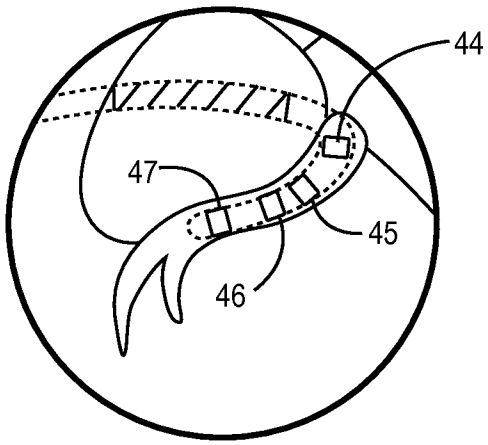
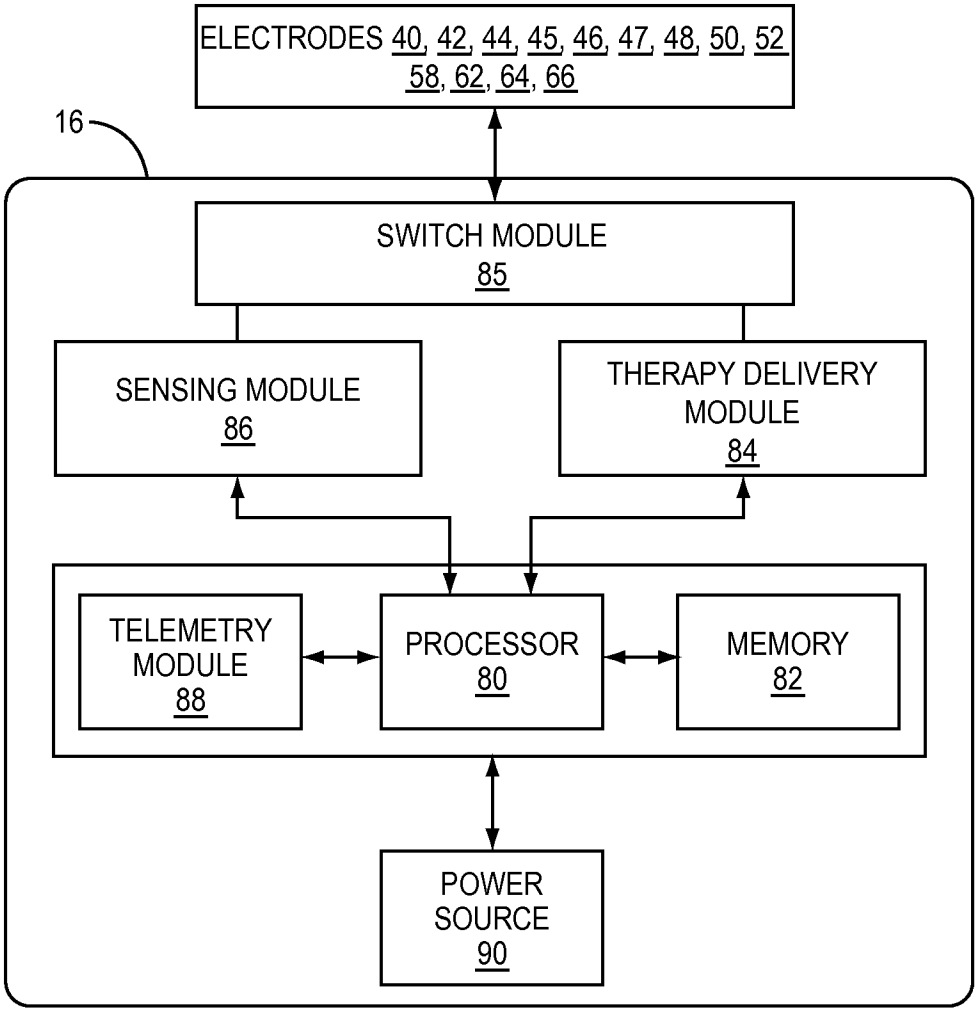


Fig. 8B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58, 62, 64, 66
16
SWITCH MODULE
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SENSING MODULE
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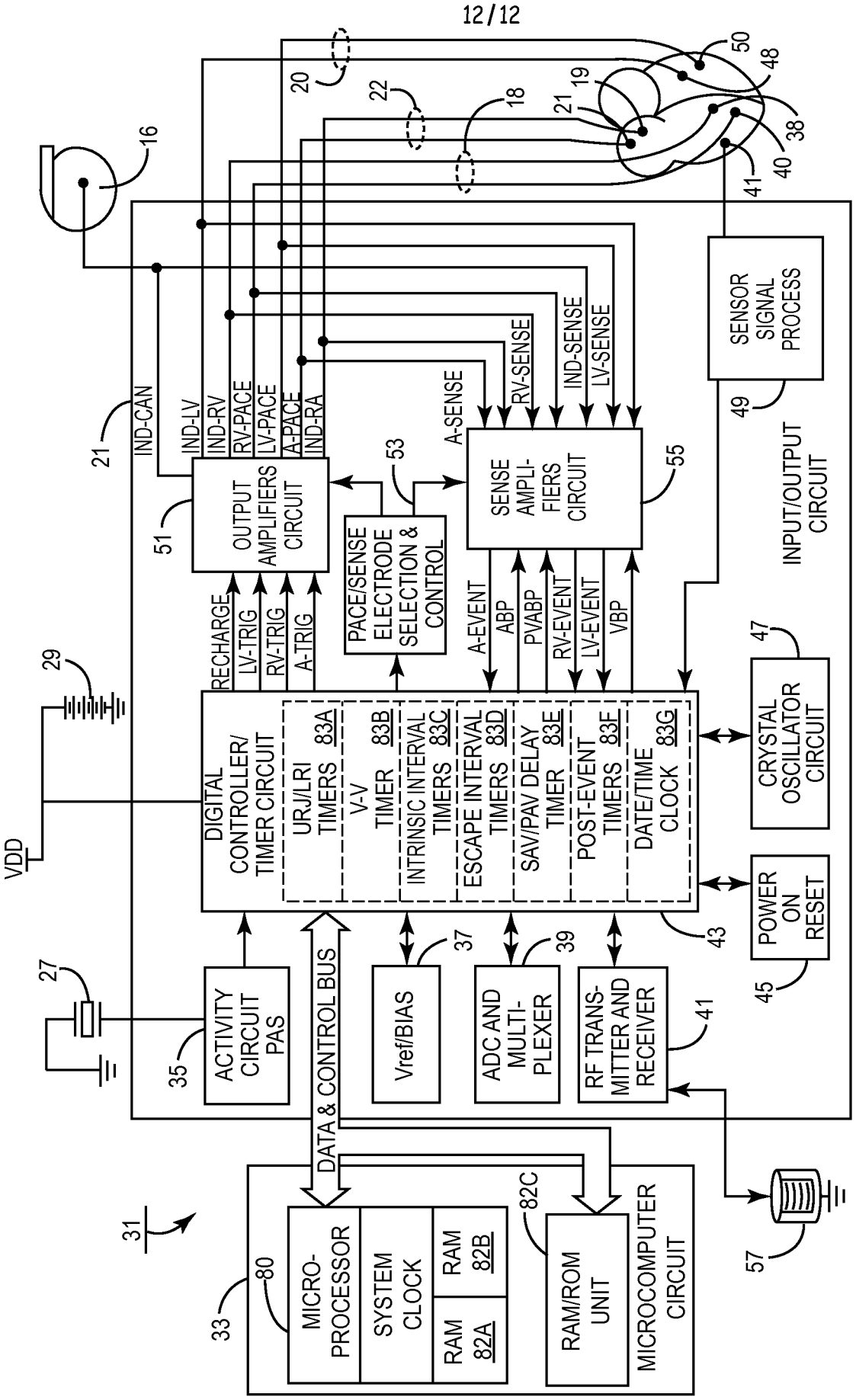
THERAPY DELIVERY
MODULE
84
TELEMETRY
MODULE
88
PROCESSOR
80
MEMORY
82
POWER
SOURCE
90

Fig. 9A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IND-CAN
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IND-LV
IND-RV
RV-PACE
LV-PACE
A-PACE
IND-RA
OUTPUT AMPLIFIERS CIRCUIT
51
53
PACE/SENSE ELECTRODE SELECTION & CONTROL
A-SENSE
RV-SENSE
IND-SENSE
LV-SENSE
SENSE AMPLI-FIERS CIRCUIT
55
SENSOR SIGNAL PROCESS
49
INPUT/OUTPUT CIRCUIT
RECHARGE
LV-TRIG
RV-TRIG
A-TRIG
A-EVENT
ABP
PVABP
RV-EVENT
LV-EVENT
VBP
29
VDD
DIGITAL CONTROLLER/ TIMER CIRCUIT
URJ/LRI TIMERS 83A
V-V TIMER 83B
INTRINSIC INTERVAL TIMERS 83C
ESCAPE INTERVAL TIMERS 83D
SAV/PAV DELAY TIMER 83E
POST-EVENT TIMERS 83F
DATE/TIME CLOCK 83G
47
CRYSTAL OSCILLATOR CIRCUIT
POWER ON RESET
45
43
27
35
ACTIVITY CIRCUIT PAS
DATA & CONTROL BUS
37
Vref/BIAS
39
ADC AND MULTI-PLEXER
41
RF TRANS-MITTER AND RECEIVER
57
31
33
80
MICRO-PROCESSOR
SYSTEM CLOCK
RAM 82B
RAM 82A
82C
RAM/ROM UNIT
MICROCOMPUTER CIRCUIT

Fig. 9B

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/048120

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/365
ADD. A61N1/362 A61N1/02 A61N1/05 A61B5/0468

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 practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1 504 713 A1 (SURGICAL NAVIGATION TECH [US]) 9 February 2005 (2005-02-09) the whole document	1-10
A	US 2008/269823 A1 (BURNES JOHN E [US] ET AL) 30 October 2008 (2008-10-30) the whole document	1-10
A	WO 2010/088040 A1 (MEDTRONIC INC [US]; KAISER DANIEL R [US]; SKADSBERG NICHOLAS D [US]; M) 5 August 2010 (2010-08-05) the whole document	1-10

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 October 2014	12/11/2014

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Edward, Vinod

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/048120

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