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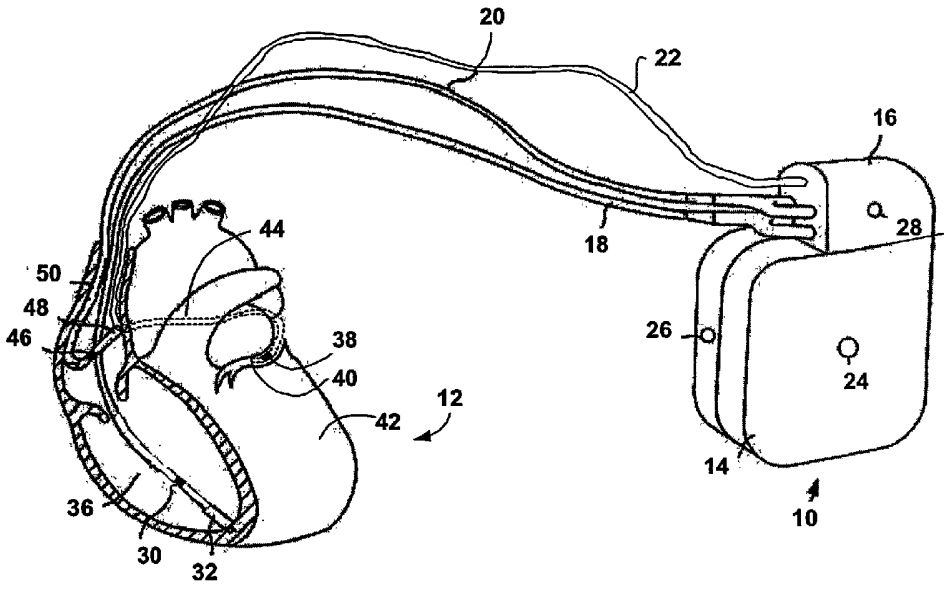
(54) Title: ISCHEMIA DETECTION BASED ON CARDIAC CONDUCTION TIME



(57) Abstract: Methods and process for detection of myocardial ischemia involve detection and analysis of changes in electrical conduction velocity within the heart to monitor changes in the condition of the cardiac muscle and indicate possible ischemia. Conduction velocity slows considerably when oxygen supply to the heart is reduced. Analysis of electrical conduction velocity can be used to verify the occurrence of myocardial ischemia in a more reliable manner. Changes in conduction velocity may be monitored based on conduction time between electrodes positioned in the left and right ventricles of the heart. The electrodes may be endocardial or epicardial electrodes. In general, the techniques may involve launching a stimulation waveform at one electrode and sensing a local cardiac depolarization at another electrode to assess conduction time.

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ISCHEMIA DETECTION BASED ON CARDIAC CONDUCTION TIME

The invention relates to cardiac health and, more particularly, to techniques for detection of myocardial ischemia.

BACKGROUND

Myocardial ischemia, a leading cause of mortality, involves oxygen starvation of the myocardium. Myocardial ischemia can lead to myocardial infarction if left untreated. Early detection of myocardial ischemia provides the opportunity for a wide range of effective therapies such as revascularization, neural stimulation, and drug delivery to reduce cardiac workload or improve cardiac circulation. Unfortunately, many episodes of myocardial ischemia do not cause excessive pain or other noticeable warning signs, and often go undetected.

An electrocardiogram (ECG) or electrogram (EGM) presents a PQRST waveform sequence that characterizes the cyclical cardiac activity of a patient. The ST segment, also associated with the repolarization of the ventricles, is typically close in amplitude to the baseline, i.e., isoelectric amplitude of the signal sensed in the TP or PQ segments. During episodes of myocardial ischemia, the ST segment amplitude often deviates from the baseline. Accordingly, deviation in the ST segment is often used to identify an occurrence of myocardial ischemia. Hence, an implantable medical device may be equipped with an ischemia detector that indicates an ischemic condition based on elevation or depression of the ST-segment relative to a baseline. Alternatively, the ischemia detector may rely on a measure of heart activity or patient workload.

Unfortunately, the use of the ST segment as an indicator of ischemia can be unreliable. The ST segment may deviate from the baseline due to other factors, causing false indications of myocardial ischemia. For example, the ST segment may deviate from the baseline due to changes in the overall PQRST complex, possibly caused by axis shifts, electrical noise, cardiac pacing stimuli, drugs and conduction aberrancy that distorts the PQRST complex. In addition, the occurrence of cardiac ischemia may not manifest as changes in the ECG or EGM signals. Consequently, the reliability of the ST segment as an indicator of myocardial ischemia can be unacceptably low.

U.S. Patent No. 6,128,526 to Stadler et al. describes an ischemia detector that observes variation in the ST segment to identify an ischemic condition. To improve reliability, the detector is designed to filter out ST segment variations caused by factors other than ischemia, such as axis shift, electrical noise, cardiac pacing, conduction aberrancy, and other distortions in the overall PQRST complex. Nevertheless, the sensitivity and specificity of ischemia detection based on observation of ST-segment changes is suboptimal. Accordingly, there continues to be a need for a simplified system capable of automatically and reliably detecting myocardial ischemia.

The invention is directed to techniques for monitoring disease-related changes in myocardial substrate with an emphasis on more reliable detection and treatment of myocardial ischemia. In particular, the techniques involve detection and analysis of changes in electrical conduction velocity within the heart to monitor changes in the condition of the heart muscle and thereby indicate possible ischemia. Conduction velocity slows considerably when oxygen supply to the heart is reduced. Thus, analysis of electrical conduction velocity or, alternatively, conduction time between two fixed electrodes in contact with the heart, can be used to verify the occurrence of myocardial ischemia in a more reliable manner. Accordingly, in the text below, the term "conduction velocity" may broadly refer to representation of electrical propagation as measured by conduction time between two individual fixed electrodes. Alternatively, the conduction time may be measured between two pairs of fixed electrodes, e.g., in a bipolar electrode arrangement.

The conduction time may be monitored between electrodes positioned in or on the left and right ventricles of the heart. The electrodes may be endocardial or epicardial electrodes. In some cases, one of the electrodes may be endocardial and another electrode may be epicardial. In general, the techniques may involve launching a wave front from a first electrode and sensing the arrival of this wave front at a second electrode to assess average conduction time across the heart tissue. More particularly, a stimulus that initiates myocardial depolarization is delivered to the first electrode or pair of electrodes. The second electrode or pair of electrodes then senses the arrival of the wave front as local cardiac depolarization. The time between launching the wave front at the first electrode(s)

and sensing the local cardiac depolarization at the second electrode(s) provides an indication of conduction velocity and, hence, the state of the cardiac tissue. Disease-related changes in myocardial substrate, e.g., manifesting in myocardial ischemia, can be detected based on changes in this time.

The techniques for analysis of conduction velocity may be implemented within an implantable medical device. A change in conduction time represents a change in conduction velocity, and may be used as an independent mode for verification of ischemia. Alternatively, changes in conduction time may be considered in combination with other measurements, such as ST segment deviation, to detect ischemia. As a further alternative, the conduction time may be considered in combination with a patient activity level, e.g., as indicated by an accelerometer signal, to distinguish changes in conduction time that occur with changes in activity level from those that occur with ischemia. The change in conduction time may be compared to a threshold for detection of ischemia. In addition, the rate of change in conduction time may be analyzed to distinguish ischemia-induced changes from anomalous changes that may be caused by other factors.

In one embodiment, the invention provides a method comprising detecting cardiac conduction time, and indicating myocardial ischemia based on the detected conduction time.

In another embodiment, the invention provides a device comprising a detector to detect cardiac conduction time, and indicate myocardial ischemia based on the detected conduction time.

In an added embodiment, the invention provides a device comprising means for detecting cardiac conduction time, and means for indicating myocardial ischemia based on the detected conduction time.

In a further embodiment, the invention provides a method comprising launching a first stimulation wave front from a first ventricular chamber, sensing a first local cardiac depolarization in a second ventricular chamber, detecting a first time between launching the first wave front and sensing the first local cardiac depolarization, launching a second stimulation wave front from the second ventricular chamber, sensing a second local cardiac depolarization in the first ventricular chamber, detecting a second time between

launching the second wave front and sensing the second local cardiac depolarization, and indicating myocardial ischemia based on the first time and the second time.

In another embodiment, the invention provides a device comprising means for launching a first stimulation wave front from a first ventricular chamber, means for sensing a first local cardiac depolarization in a second ventricular chamber, means for detecting a first time between launching the first wave front and sensing the first local cardiac depolarization, means for launching a second stimulation wave front from the second ventricular chamber, means for sensing a second local cardiac depolarization in the first ventricular chamber, means for detecting a second time between launching the second wave front and sensing the second local cardiac depolarization, and means for indicating myocardial ischemia based on the first time and the second time.

The invention may provide a number of advantages. In accordance with the invention, detection of changes in electrical conduction velocity within the heart, e.g., via measurement of conduction time, may provide a more reliable indication of an ischemic episode. In particular, the invention may be useful in increasing the specificity of ischemia detection, generally avoiding false indication of ischemic events due to axis shifts, electrical noise, cardiac pacing stimuli, high sinus or tachycardia rates, or other factors that undermine the effectiveness of existing techniques such as ST segment deviation analysis. The invention may also be useful in increasing the sensitivity of ischemia detection by detecting some ischemia episodes that are not manifested in ECG or EGM waveforms. In addition, in some embodiments, the invention can be useful in quantifying a degree or severity of ischemic tissue according to the amount and/or rate of change in conduction time.

The above summary of the invention is not intended to describe every embodiment of the invention. The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

FIG. 1 is a diagram illustrating an exemplary implantable medical device in association with a heart.

FIG. 2 is a block diagram illustrating a device for detection of ischemia.

FIG. 3 is a block diagram illustrating a device for detection of ischemia and delivery of therapy.

FIG. 4 is a flow diagram illustrating a technique for detection of ischemia based on cardiac conduction time.

FIG. 5 is a flow diagram illustrating another technique for detection of ischemia based on cardiac conduction time.

FIG. 6 is a flow diagram illustrating a further technique for detection of ischemia based on cardiac conduction time.

FIG. 7 is a flow diagram illustrating a technique for detection of ischemia based on cardiac conduction time and ST segment deviation.

FIG. 8 is a flow diagram illustrating a process for detection of ischemia based on cardiac conduction time and morphology of a waveform used to measure conduction time.

FIG. 9 is a flow diagram illustrating a process for detection of ischemia based on cardiac conduction time and activity level.

FIG. 10 is a flow diagram illustrating a process for detection of ischemia based on cardiac conduction time between the right ventricle and left ventricle and cardiac conduction time between the left ventricle and the right ventricle.

FIG. 11 is a flow diagram illustrating a process for detection of ischemia based on a difference between cardiac conduction time between the right ventricle and left ventricle and cardiac conduction time between the left ventricle and the right ventricle.

FIG. 1 is a diagram illustrating an exemplary implantable medical device (IMD) 10 in association with a human heart 12. IMD 10 may be dedicated to monitoring of heart 12, or integrate both monitoring and therapy features, as will be described. In accordance with the invention, IMD 10 is configured to detect cardiac conduction velocity, via measurement of conduction time, and detect myocardial ischemia based on the detected conduction time. Using conduction time, IMD 10 detects changes in the state of heart 12, and thereby obtains an indication of heart tissue conditions suggestive of myocardial ischemia within the heart 12.

When a change in cardiac conduction time reveals ischemic conditions, IMD 10 indicates an ischemic episode. Conduction velocity across cardiac muscle tends to decrease significantly when oxygen supply to the heart is reduced. At the same time, conduction time tends to increase. Consequently, the conduction time between two fixed electrodes can provide a good indication of cardiac ischemia. In some embodiments, IMD 10 may monitor both conduction time changes and other parameters such as ST segment deviation from a baseline and patient activity level to identify an ischemic episode.

If ischemia is detected, IMD 10 may deliver appropriate therapy to alleviate its effects. The therapy may include drug delivery, electrical stimulation, or both. In addition, the therapy may be delivered directly by IMD 10 or by other devices in response to indication of ischemia by the IMD. In addition, according to some embodiments, IMD 10 may be configured to determine the degree of severity of the ischemic condition, providing more specific information that may be useful in selection of particular therapies. For example, IMD 10 may quantify a change in conduction time and estimate the extent of ischemia as a function of the quantity. In this case, IMD 10 may select a particular therapy, or select a level of stimulation or drug delivery associated with the therapy, according to the estimated degree of severity of the ischemic episode.

As shown in FIG. 1, IMD 10 may be generally flat and thin to permit subcutaneous implantation within a human body, e.g., within upper thoracic regions or the lower abdominal region. IMD 10 may include a hermetically sealed housing 14 having a connector block assembly 16 that receives the proximal ends of one or more cardiac leads for connection to circuitry enclosed within the housing. In the example of FIG. 1, connector block assembly 16 receives three cardiac leads. In particular, connector block assembly 16 receives a right ventricular endocardial lead 18, a left ventricular epicardial lead 22, and a right atrial endocardial lead 20. In addition, housing 14 may function as an electrode, along with a set of electrodes 24, 26, 28 provided at various locations on the housing or connector block assembly 16.

Ventricular leads 18, 22 may include, in some embodiments, pacing electrodes and defibrillation coil electrodes (not shown) in the event IMD 10 is configured to provide pacing, cardioversion and defibrillation. In addition, ventricular leads 18, 22 may deliver pacing stimuli in a coordinated fashion to provide biventricular pacing and cardiac

resynchronization. Electrodes 24, 26, 28 may form a variety of sensing pairs with electrodes carried by leads 18, 20, 22 to obtain different sets of desired EGM data for heart 12.

To detect cardiac conduction time, in accordance with the invention, right ventricular lead 18 includes a signal transmitting electrode 32 adjacent a distal end of the right ventricular lead within right ventricle 36 of heart 12. Right ventricular lead 18 may carry other sense or stimulation electrodes, such as electrode 30 shown in FIG. 1. In addition, left ventricular lead 22 includes a signal sensing electrode 38 adjacent a distal end 40 of the left ventricular lead. Electrodes 32, 38 transmit and sense electrical potentials in relation to a reference electrode, which may be carried on IMD 10, e.g., as part of housing 14. Alternatively, the reference electrode may be provided as part of a bipolar electrode configuration carried by the respective lead 18, 22. Left ventricular lead 22 may be deployed to contact left ventricle 42 via the coronary sinus and coronary vein 44. Atrial lead 20 may be provided to permit atrial sensing, and may include an electrode 46 adjacent a distal end 48 of the right atrial lead within right atrium 50.

In operation IMD 10 drives signal transmitting electrode 32 via right ventricular lead 18 to apply a stimulation wave front to right ventricle 36. The wave front is selected to have an amplitude and pulse width sufficient to initiate myocardial depolarization in right ventricle 36. Sensing electrode 38 senses a localized cardiac depolarization in left ventricle 42 upon propagation of the depolarization wave front from right ventricle 36, and communicates the sensed signal to IMD 10 via left ventricular lead 22. IMD 10 may include sensor circuitry to process the received signal. In addition, IMD 10 may include detector circuitry to determine a conduction time based on the time delay between application of the stimulation wave front in right ventricle 36 and sensing of the local depolarization in left ventricle 42. In this manner, the detection circuitry permits detection of myocardial ischemia based on a change in the detected conduction time.

The cardiac conduction time varies as a function of the condition of tissue within heart 12, and provides an indication of ischemia. The ischemic condition can be treated, e.g., by intervention of a physician or in an automated manner. For example, upon detection of the ischemic condition, IMD 10 may activate an alarm. Alternatively or in addition to alarm activation, IMD 10 may select a therapy and coordinate the delivery of

the therapy by IMD or some other device. In addition, in the event the therapy involves electrical stimulation, the amplitude, frequency, or pulse width of stimulating current can be controlled according to the indicated degree of ischemia to achieve an optimum therapeutic effect. As a further alternative, determination of the severity of ischemic tissue can be used to choose other types of therapy such as drug delivery, as well as types, dosages and durations of drug delivery.

FIG. 2 is a block diagram illustrating an IMD 10 configured for detection of ischemia based on heart tissue conduction time, in accordance with the invention. As shown in FIG. 2 device 10 may include a processor 52 that controls the application of the stimulation wave front in right ventricle 36 and sensing of a localized depolarization in left ventricle 42 to evaluate cardiac conduction time across tissue between electrodes within the right and left ventricles 36, 42 of heart 12. Processor 52 may be realized by a microprocessor, digital signal processor, ASIC, FPGA, or other integrated or discrete logic circuitry programmed or otherwise configured to provide functionality as described herein.

Processor 52 may function to provide, for example, a controller 54 and an ischemia detector 56. Controller 54 and ischemia detector 56 may be programmable features or functional blocks of processor 52. Controller 54 controls the operation of right ventricular signal generator circuitry 58. Signal generator circuitry 58, in response to a control signal from controller 54, launches a stimulation wave front into right ventricle 36 via signal transmitting electrode 32 of right ventricular lead 18.

For patients with little or no intrinsic rhythm, such as patients with second or third degree AV conduction block, that are paced for a majority or all of the time, the stimulation wave front can be readily coordinated with pacing pulses. In particular, right ventricular pacing pulses may be used as the stimulation wave front that initiates a myocardial depolarization in right ventricle 36, which then propagates across the cardiac tissue to cause a local depolarization in left ventricle 42. In patients with normal sinus activity, overdrive pacing slightly above the sinus rate can be performed at regular intervals to obtain the conduction times. The time interval for measurements can be a programmable parameter of IMD 10, which may be patient specific and set at the discretion of the physician.

Left ventricular sensor circuitry 60, coupled to left ventricular lead 22, captures the sensed depolarization received at measurement electrode 38. Sensor circuitry 60 may amplify, condition and digitize the depolarization signal, and provide the signal in digital form to ischemia detector 56. In some embodiments, sensor circuitry 60 may merely present to ischemia detector 56 a timing signal indicative of the arrival of the depolarization at measurement electrode 38 for comparison to the transmission time of the stimulation wave front at transmitting electrode 32.

As an alternative to transmission of the stimulation wave front via right ventricular lead 18 and sensing via left ventricular lead 22, the left ventricular lead could be equipped with a set of bipolar epicardial electrodes. In this case, conduction time can be measured at the surface of the left ventricle 42 by transmitting a stimulation wave front between the bipolar electrodes of left ventricular lead 22. The bipolar electrodes may be disposed at different axial positions along the length of left ventricular lead 22, and may be approximately 1 to 2 cm apart from one another.

An epicardial arrangement may be particularly effective in identifying the onset of ischemia because the effect of ischemia is first felt in the epicardial layers of the cardiac tissue. As a result, changes in conduction time between a pair of epicardial electrodes carried by left ventricular lead 22 may serve to provide an early warning of ischemia. Moreover, proximity of a pair of left ventricular epicardial electrodes to the left anterior descending (LAD) and circumflex arteries, the two most commonly occluded arteries, would make such a configuration particularly sensitive to ischemia detection.

In operation, ischemia detector 56 tracks the time the stimulation wave front was applied by right ventricular lead 18 and the time the resulting depolarization was sensed by left ventricular lead 22 to determine the conduction time across the heart tissue between right and left ventricles 36, 42 of heart 12. As ischemia sets in, and the conduction velocity progressively decreases, the conduction times between the two electrodes on leads 18, 22 will increase.

Ischemia can be detected when the conduction time is longer than a threshold value. The threshold value may be a nominal value derived from a typical implanted cardioverter-defibrillator device (ICD) population of patients. Alternatively, the threshold value may be independently adjusted and set for a given patient as desired by the attending

physician. For diagnosis purposes, the more recent values of the conduction time, e.g., with a time and date stamp, as well as other information, may be stored in a memory associated with IMD 10 along with the most recent arrhythmia to facilitate diagnosis of any association between the onset of ischemia and arrhythmia episodes.

Over a period of time, processor 52 may collect a series of conduction time samples as a function of the measured conduction time. With each sample, ischemia detector 56 compares the conduction time to a baseline conduction time evaluated in one or more previous samples to identify a change in conduction time. The baseline conduction time may be updated over time. For example, the baseline conduction time may represent a mean or median conduction time over a period of n preceding samples.

When the change in conduction time exceeds a predetermined threshold, ischemia detector 56 indicates an ischemic condition within heart 12 and generates an ischemia signal. The change in conduction time may be measured based on a single sample, or based on the mean or median conduction time change over a series of samples. The ischemia signal may be used to drive selection and delivery of one or more therapies.

FIG. 3 is a block diagram illustrating an IMD 10' configured for detection of ischemia and delivery of therapy. IMD 10' of FIG. 3 corresponds substantially to IMD 10 of FIG. 2, but further includes both a therapy control circuit 62 that drives a therapy delivery system 64, and a telemetry circuitry 65 that drives an antenna 66. IMD 10 also may include an activity level sensor 63 to indicate a level of physical activity of a patient in which the IMD is implanted. Activity level sensor 63 may include, for example, an accelerometer. When ischemia detector 56 detects a change in conduction time that exceeds a threshold, it transmits an ischemia signal to therapy control circuitry 62, which may interact with a therapy delivery system 64 within IMD 10' or associated with another device, or both.

Therapy delivery system 64 may take the form of a drug delivery system or electrical stimulation system such as a neurostimulation, pacing, cardioversion or defibrillation circuit. For example, in some embodiments, therapy control circuitry 62 may interact with an electrical stimulation therapy device integrated with IMD 10' to deliver pacing, post-extrasystolic potentiation, cardioversion or defibrillation therapy, and also communicate with a drug delivery device that may be implanted or external to deliver

drug therapy to the patient. In addition, telemetry circuitry 65 may alert an external monitoring system by wireless communication via antenna 66. IMD 10' also may include internal alarm circuitry 67 that is responsive to the ischemia signal produced by ischemia detection circuitry 56.

In addition, in some embodiments, ischemia detector 56 of IMD 10' as described herein may include electrocardiogram signal analysis circuitry for identifying deviation of the ST segment of the electrocardiogram as an indication of ischemia. In this manner, IMD 10' may analyze both conduction time and ST segment deviation to detect ischemia. If IMD 10' detects an ST segment deviation greater than a given ST threshold, for example, in combination with a conduction time change that exceeds another threshold, IMD 10' may identify an ischemic episode. In this manner, the conduction time change can provide confirmation that the ST segment deviation is due to an ischemic condition, rather than an anomalous ST segment deviation caused by factors other than ischemia. Alternatively, the sensitivity to ischemia could be increased by identifying an ischemic episode when either the conduction time or an ST-segment deviation are detected.

Based on the amount of conduction time change, IMD 10 also may quantify the severity of the ischemic condition. In some embodiments, the ischemia signal transmitted by ischemia detector 60 may specify selection of a particular type of therapy, e.g., drug delivery and/or electrical stimulation, as well as the level, dosage, amplitude, and duration of the therapy, based on the indications of the severity of the ischemic condition determined from the amount of conduction time change.

Telemetry circuitry 65, as discussed above, communicates an indication of the ischemic condition to an external device via antenna 66. Thus, the indication may be a wireless, radio frequency message that indicates an ischemic condition and, in some embodiments, the severity of the ischemic condition. In addition, IMD 10' itself may have an audible alarm within alarm circuitry 67 that notifies the patient when an ischemic episode is occurring. The external device that receives the wireless message may be a programmer/output device that advises a physician or other attendant of the ischemic condition, e.g., via a display or a visible or audible alarm. Also, the ischemic events may be stored in memory in the external device, or within the IMD 10', for review by a physician.

The components of IMD 10, with the exception of leads 18, 22, may be housed in a common housing such as that shown in FIG. 1. Alternatively, portions of IMD 10' may be housed separately. For example, therapy delivery system 64 could be integrated with IMD 10' or provided in a separate housing, particularly where the therapy delivery system includes drug delivery capabilities. In this case, therapy control circuit 62 may interact with therapy delivery system 64 via an electrical cable or wireless link.

FIG. 4 is a flow diagram illustrating a technique for detection of ischemia based on conduction time. In general, the process may include launching a stimulation wave front from the right ventricular lead 18 (68), detecting a local cardiac depolarization at the left ventricular lead 22 (70), and measuring the conduction time between the right and left ventricular leads 18, 22 (72). The conduction time may be determined based on the time required for the depolarization initiated by the stimulation wave front to propagate across the heart tissue from right ventricular lead 18 to left ventricular lead 22 and cause a depolarization in left ventricle 42.

In the example of FIG. 4, the stimulation wave front is transmitted from the right ventricular endocardial lead 18, with the resulting depolarization being sensed by the left ventricular epicardial lead 22. However, an opposite arrangement may be used in which the stimulation wave front is transmitted from the left ventricular epicardial lead 22, and the resulting depolarization is sensed by the right ventricular endocardial lead 18. Moreover, in some embodiments, both leads may be endocardial leads, or both leads may be epicardial leads.

The process involves determining conduction time and then comparing the conduction time to a threshold conduction time (74). More specifically, in certain embodiments, the process compares a change in the conduction time to a change threshold. Again, the change in conduction time may be determined by comparing a mean or median conduction time over a series of samples to a mean or median conduction time for a preceding series of samples. If the change in conduction time exceeds the threshold (74), the process indicates ischemia (76). In some embodiments, the comparison of the conduction time to a threshold may be accompanied by analysis of ST segment deviation or other parameters that may also be indicative of an ischemic episode. Upon detection of

an ischemic episode, the process further may involve delivery of therapy (77) and activation of an alarm (79).

FIG. 5 is a flow diagram illustrating another process for detection of ischemia based on conduction time. In the example of FIG. 5, the process involves launching a stimulation wave front from the right ventricular lead 18 (78), detecting the resulting depolarization at the left ventricular lead 22 (80), and measuring the conduction time between the right and left ventricular leads 18, 22 (82). Again, the stimulation wave front alternatively may be transmitted from the left ventricular lead 22, with the depolarization sensed at the right ventricular lead 18, and the process is subject to variation in the endocardial or epicardial arrangement of the leads. The process next determines whether the conduction time change is greater than a given threshold (84). In the example of FIG. 5, the process may rely on a static threshold that does not take into account the conduction time associated with previous samples.

If the conduction time change is greater than an applicable threshold (84), the process next measures the slope of the conduction time change (86). The slope of the conduction time change over time can serve to distinguish changes that are indicative of ischemia from spurious changes that may arise due to other factors. For example, many non-ischemic conditions such as drug therapy, changes in electrolyte concentrations, temperature changes, progression of disease, and the like may influence myocardial conduction time very slowly. Conversely, fusion of stimulated and intrinsic depolarization wave fronts, conduction aberrancy, electrode motion or dislodgement, and the like may influence the measured conduction time very rapidly. For these reasons, the rate of change (i.e., slope) of the conduction time over time may serve to distinguish among various factors influencing conduction time.

To improve the specificity of ischemic detection based on conduction time, the process may be configured to exclude non-ischemic etiology of changes in conduction time by accepting only specific rates of change of the conduction time as being indicative of ischemia. If the conduction time slope falls outside of a desired range (88), i.e., the rate of change is too slow or too fast, the process ignores the conduction time change and does not indicate an ischemic episode. If the conduction time slope is within the desired range,

however, the process indicates ischemia (90). In this case, IMD 10 may direct delivery of therapy (91) and activation of an alarm (93).

An increase in conduction time that is caused by ischemia will tend to follow a known time course, typically resulting in a fifty percent increase in conduction time over a period of one to ten minutes. An increase in conduction time that occurs faster than such a rate generally is not caused by ischemia. Rather, the likely cause of the increase in conduction time will be a conduction aberrancy, electrode motion or dislodgement, or conduction block in a section of the myocardium that is refractory. To avoid the possibility of encountering refractive myocardium, it may be desirable to avoid transmission of the stimulation wave front prematurely or immediately following a premature ventricular contraction.

An increase in conduction time that occurs over a time period longer than approximately ten minutes also generally is not caused by ischemia. Instead, the likely cause of slow changes in conduction time are changes in electrolytes, medications or progression of disease. Accordingly, it may be desirable to exclude changes in conduction time that are too slow or too fast to be caused by ischemia, as served by the slope comparison (88).

To exclude slow, drifting changes in conduction time, a baseline conduction time, i.e., a normal expected conduction time, may be allowed to change slowly over time. A baseline conduction time may be established over a series of conduction time measurement samples. Observation of an ischemic change then becomes an observation of a change in conduction time relative to the adaptive baseline conduction time. To exclude fast, sudden changes in conduction time, an adaptive expected range of conduction times can be established. The expected range could be composed, for example, of an adaptive mean of conduction time +/- an adaptive estimate of the variability of conduction times. Measurements of conduction time that occur outside of the expected range may be excluded as outliers. If consecutive measurements are consistently excluded as outliers, a new expected range of conduction times, based on this new steady state value, can be established.

FIG. 6 is a flow diagram illustrating a further process for detection of ischemia based on conduction time. The process illustrated in FIG. 6 may correspond substantially

to the process of FIG. 5. Instead of using a static conduction time change threshold, however, the process makes use of a dynamic conduction time change threshold that varies as a function of recent conduction time samples. Accordingly, as shown in FIG. 6, the process involves launching a stimulation wave front from the right ventricular lead 18 (92), detecting arrival of the resulting depolarization at the left ventricular lead 22 (94), and measuring the conduction time between the right and left ventricular leads 18, 22 (96).

The process next determines a slope of the conduction time over a series of recent conduction time samples (98). Based on the slope, the process modifies the threshold value of conduction time change (100). In this manner, the process adapts the threshold value for conduction time change to the rate of change in the measured conduction time. If the measured conduction time changes more rapidly, the process may involve increasing the threshold level of the conduction time change for ischemia detection. If the conduction time changes more slowly, the process may involve decreasing the threshold level of the conduction time change for ischemia detection.

The dynamic threshold serves to adapt the process to changing conditions in the conduction time, and can help to avoid detection of ischemia based on momentary, spurious shifts in conduction time. For example, if the conduction time changes abruptly, the level of the conduction time threshold may be increased to require a larger change. If the conduction time change exceeds the threshold (102), the process detects ischemia (104). In response, IMD 10 may direct delivery of therapy and activation of an alarm (such as alarm 67 in FIG. 3).

FIG. 7 is a flow diagram illustrating a process for detection of ischemia based on conduction time and ST deviation. As shown in FIG. 7, the process involves launching a wave front from the right ventricular lead 18 (106), detecting the conducted wave front at the left ventricular lead 22 (108), and measuring the conduction time between the right and left ventricular leads 18, 22 (110). If the conduction time change exceeds an applicable threshold (112), the process analyzes the ST segment to identify ST deviation from isoelectric (114) and thereby corroborate the ischemic condition indicated by the change in conduction time. If ST deviation greater than a particular level exists, the process indicates ischemia (116), and may direct delivery of therapy and activation of an alarm system. In some embodiments, the process of FIG. 7 may be modified such that ischemia

is indicated when either the conduction time change exceeds an applicable threshold or ST deviation is encountered. In this manner, ischemia is indicated in response to either criterion such that the ischemia detection process is less selective but more inclusive, and therefore less likely to miss detection of an ischemic episode.

FIG. 8 is a flow diagram illustrating a process for detection of ischemia based on conduction time and waveform morphology. The process of FIG. 8 conforms substantially to the process of FIG. 7. For example, the process of FIG. 8 involves launching a stimulation wave front from the right ventricular lead 18 (118), detecting a resulting depolarization at the left ventricular lead 22 (120), and measuring the conduction time between the right and left ventricular leads 18, 22 (122).

If the conduction time change exceeds an applicable threshold (124), the process further evaluates the morphology of the measured signal waveform, i.e., the sensed depolarization wave form, as an alternative or in addition to ST segment analysis. In particular, processor 52 in IMD 10 may be equipped to perform wavelet analysis of other waveform analysis techniques to analyze the morphology of the depolarization signal or other cardiac waveforms within heart 12. If the morphology matches a template corresponding to a normal morphology (126), the process does not detect ischemia. If the morphology does not match the template (126), i.e., differs significantly from the template, and the conduction time change exceeds the threshold (124), the process indicates ischemia (128).

In this example, analysis of waveform morphology for the depolarization signal received at left ventricular lead 22 serves to corroborate the ischemic condition indicated by the change in conduction time. During ischemia, a broadening of the detected waveform may be expected as the conduction becomes more fractionated. Accordingly, tools such as wavelet analysis may be useful in matching the detected activity against a normal template. A deviation from the template that exceeds a programmed threshold, e.g., waveform width, amplitude, energy, or the like, can be use to signal ischemia or other deleterious changes in the myocardium.

FIG. 9 is a flow diagram illustrating a process for detection of ischemia based on conduction time and activity level. As shown in FIG. 9, the process involves launching a stimulation wave front from the right ventricular lead 18 (130), detecting a resulting

depolarization at the left ventricular lead 22 (132), and measuring the conduction time between the right and left ventricular leads 18, 22 (134). If the conduction time change exceeds an applicable threshold (136), the process further involves obtaining an activity level (137), e.g., from an activity level sensor 63 (FIG. 3). The activity level can help to distinguish changes in conduction time that occur with changes in activity level from those changes in conduction time that occur with ischemia. In general, if a patient is ischemic, the conduction time should increase with either no change or an increase in activity level. If a patient is not ischemic, however, increases in conduction time should occur only with decreases in activity level. Accordingly, if the activity level is greater than or equal to a threshold (138), the process indicates ischemia (140). If the activity level is less than the threshold, ischemia is not indicated.

FIG. 10 is a flow diagram illustrating a process for detection of ischemia based on both conduction time between the right ventricle and left ventricle (RV-LV) and conduction time between the left ventricle and the right ventricle (LV-RV). As shown in FIG. 10, the process involves launching a stimulation wave front from the right ventricular lead 18 (142), detecting a resulting depolarization at the left ventricular lead 22 (144), and measuring the conduction time between the right and left ventricular leads 18, 22 (146). If the RV-LV conduction time change exceeds an applicable threshold (148), the process further involves launching a stimulation wave front from the left ventricular lead 22 (150), detecting a resulting depolarization at the right ventricular lead 18 (152), and measuring the conduction time between the left and right ventricular leads 22, 18 (154). If the LV-RV conduction time change also exceeds an applicable threshold (156), the process indicates ischemia (158).

FIG. 11 is a flow diagram illustrating a process for detection of ischemia based on a difference between conduction time between the right ventricle and left ventricle and conduction time between the left ventricle and the right ventricle. As shown in FIG. 11, the process involves launching a stimulation wave front from the right ventricular lead 18 (160), detecting a resulting depolarization at the left ventricular lead 22 (162), and measuring the conduction time between the right and left ventricular leads 18, 22 (164). The process further involves launching a stimulation wave front from the left ventricular lead 22 (166), detecting a resulting depolarization at the right ventricular lead 18 (168),

and measuring the conduction time between the left and right ventricular leads 22, 18 (170). Upon computing the difference between the LV-RV conduction time and the LV-RV conduction time (172), the process determines whether the difference is greater than a predetermined threshold (174). A significant difference may be an indication of an ischemic condition that has altered the conductive state of the cardiac tissues. Accordingly, if the difference is greater than the predetermined threshold, ischemia is indicated (176).

Additional variations to the embodiments of the invention described herein are also conceivable. For example, as mentioned previously, the stimulation wave front used to measure conduction time may be launched between a variety of lead arrangements, including right endocardial to left endocardial, left endocardial to right endocardial, right endocardial to left epicardial, left epicardial to right endocardial, right epicardial to left epicardial, left epicardial to right epicardial, left bipolar epicardial, and the like.

In addition, the stimulation wave front may be transmitted as part of a pacing pulse or other therapy pulses or as a dedicated measurement pulse. The stimulation wave front may be transmitted alternatively from the right to the left lead or from the left to the right lead on successive measurement cycles during a single monitoring session to improve sensitivity and specificity for ischemia detection.

As further variations, multiple bipolar electrodes on a single lead may be provided and selected for use in the measurement of conduction time depending on the particular patient's condition, e.g., to be more selectively directed to an area of the heart known to be prone to ischemia. In particular, factors such as location of a previous ischemic condition may affect the location of the optimum transmitting or measurement electrode, or both.

In patients with bi-ventricular pacing, suspension of right ventricular pacing while performing left ventricular pacing could be used to measure conduction time. If appropriate, pacing from the right ventricle and measurement of the depolarization in the left ventricle can be used in some patient populations.

In extreme cases of ischemia, lack of left ventricular or right ventricular capture may occur depending on the location of the ischemic region if the electrode happens to be located inside the ischemic region. In some cases, loss of capture may be used as a rough tool to initially identify the location of an ischemic region.

Further, if the patent has a good sinus rhythm, overdrive pacing from one of the locations for a small number of beats may be desirable so that atrial activity and fusion beats do not confound the conduction time measurements. In patients with regular rhythm, one way to prevent incoming atrial activity from undermining the conduction time measurement may be to perform vagal stimulation, if available, or use other means to temporarily prevent AV conduction.

In many cases, the best location for the right ventricular lead may be determined experimentally, e.g., by performing acute occlusion of an artery that seems most likely to suffer from plaque rupture. In some patients, the right ventricular septal location may be the optimum location for conduction time measurement.

Various embodiments of the invention have been described. These and other embodiments are within the scope of the following claims.

What is claimed is:

1. A method comprising:

detecting cardiac conduction time; and

indicating myocardial ischemia based on the detected conduction time.

2. The method of claim 1, further comprising:

launching a stimulation wave front from a first electrode positioned proximate a first ventricular chamber; and

sensing a local cardiac depolarization at a second electrode positioned proximate a second ventricular chamber,

wherein detecting cardiac conduction time includes detecting a time between launching the wave front and sensing the local cardiac depolarization.

3. The method of claim 2, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an epicardial electrode positioned on a surface of the second ventricular chamber.

4. The method of claim 2, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an endocardial electrode positioned within the second ventricular chamber.

5. The method of claim 2, wherein the first electrode includes an epicardial electrode positioned on a surface of the first ventricular chamber, and the second electrode includes an epicardial electrode positioned on a surface of the second ventricular chamber.

6. The method of claim 2, wherein the first ventricular chamber is the right ventricular chamber and the second ventricular chamber is the left ventricular chamber.

7. The method of claim 2, wherein the first ventricular chamber is the left ventricular chamber and the second ventricular chamber is the right ventricular chamber.

8. The method of claim 1, wherein indicating myocardial ischemia includes:

comparing the detected conduction time to a threshold conduction time; and

indicating ischemia when the detected conduction time exceeds the threshold conduction time.

9. The method of claim 8, further comprising adjusting the threshold conduction time based on a rate of change of the conduction time.

10. The method of claim 1, wherein detecting myocardial ischemia includes:
comparing the detected conduction time to a threshold conduction time;
comparing a rate of change of the detected conduction time to a range of change; and
indicating ischemia when the detected conduction time exceeds the threshold conduction time and the rate of change of the detected conduction time is within the range of change.

11. The method of claim 1, wherein indicating myocardial ischemia includes:
determining a rate of change of the detected conduction time; and
indicating ischemia based on the rate of change.

12. The method of claim 1, further comprising detecting the conduction time using at least one lead associated with an implantable medical device.

13. The method of claim 1, further comprising, when myocardial ischemia is indicated, generating a signal for delivery of therapy to alleviate effects of the ischemia within the heart.

14. The method of claim 1, further comprising, when myocardial ischemia is indicated, storing information about the myocardial ischemia for review by a physician.

15. The method of claim 1, further comprising, when myocardial ischemia is indicated, notifying a patient.

16. The method of claim 1, further comprising, when myocardial ischemia is indicated, delivering therapy to alleviate effects of the ischemia within the heart.

17. The method of claim 16, wherein the therapy includes at least one of drug delivery, electrical stimulation, modification of ongoing electrical stimulation, and a combination of drug delivery and electrical stimulation.

18. The method of claim 1, further comprising quantifying a degree of ischemia based on the detected conduction time.

19. The method of claim 1, further comprising:
detecting ST deviation; and
indicating myocardial ischemia based on the detected conduction time and the detected ST deviation.

20. The method of claim 1, further comprising:
launching a stimulation wave front from a first electrode positioned proximate a first ventricular chamber;

sensing a local cardiac depolarization at a second electrode positioned proximate a second ventricular chamber; and

evaluating a morphology of a waveform associated with the sensed depolarization,

wherein detecting cardiac conduction time includes detecting a time between launching the wave front and sensing the local cardiac depolarization, and indicating myocardial ischemia includes indicating myocardial ischemia based on the detected conduction time and the morphology.

21. The method of claim 1, further comprising:

detecting an activity level of a patient; and

indicating myocardial ischemia based on the detected conduction time and the detected activity level.

22. A device comprising a detector to detect cardiac conduction time, and indicate myocardial ischemia based on the detected conduction time.

23. The device of claim 22, further comprising:

a first electrode positioned proximate a first ventricular chamber to launch a stimulation wave front; and

a second electrode positioned proximate a second ventricular chamber to sense a local cardiac depolarization,

wherein the detector detects the cardiac conduction time based on a time between launching the wave front and sensing the local cardiac depolarization.

24. The device of claim 23, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an epicardial electrode positioned on a surface of the second ventricular chamber.

25. The device of claim 23, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an endocardial electrode positioned within the second ventricular chamber.

26. The device of claim 23, wherein the first electrode includes an epicardial electrode positioned on a surface of the first ventricular chamber, and the second electrode includes an epicardial electrode positioned on a surface of the second ventricular chamber.

27. The device of claim 23, wherein the first ventricular chamber is the right ventricular chamber and the second ventricular chamber is the left ventricular chamber.

28. The device of claim 23, wherein the first ventricular chamber is the left ventricular chamber and the second ventricular chamber is the right ventricular chamber.

29. The device of claim 22, wherein the detector compares the detected conduction time to a threshold conduction time, and indicates ischemia when the detected conduction time exceeds the threshold conduction time.

30. The device of claim 29, wherein the detector adjusts the threshold conduction time based on a rate of change of the conduction time.

31. The device of claim 22, wherein the detector:

compares the detected conduction time to a threshold conduction time;

compares a rate of change of the detected conduction time to a threshold rate of change; and

indicates ischemia when the detected conduction time exceeds the threshold conduction time and the rate of change of the detected conduction time is less than the threshold rate of change.

32. The device of claim 22, wherein the detector senses the conduction time using at least one lead associated with an implantable medical device.

33. The device of claim 22, wherein the detector generates a signal for delivery of therapy to alleviate effects of the ischemia within the heart when myocardial ischemia is indicated.

34. The device of claim 22, further comprising a memory to store information about the myocardial ischemia for review by a physician.

35. The device of claim 22, further comprising an alarm to notify a patient when myocardial ischemia is indicated.

36. The device of claim 22, further comprising a device to deliver therapy to alleviate effects of the ischemia within the heart when myocardial ischemia is indicated.

37. The device of claim 36, wherein the therapy includes at least one of drug delivery, electrical stimulation, modification of ongoing electrical stimulation, and a combination of drug delivery and electrical stimulation.

38. The device of claim 22, wherein the detector quantifies a degree of ischemia based on the detected conduction time.

39. The device of claim 32, wherein the detector detects ST deviation, and indicates myocardial ischemia based on the detected conduction time and the detected ST deviation.

40. The device of claim 22, further comprising:

a first electrode positioned proximate a first ventricular chamber to launch a stimulation wave front; and

a second electrode positioned proximate a second ventricular chamber to sense a local cardiac depolarization,

wherein the detector evaluates a morphology of a waveform associated with the sensed depolarization, detects the cardiac conduction time based on a time between launching the wave front and sensing the local cardiac depolarization, and indicates myocardial ischemia based on the detected conduction time and the morphology.

41. The device of claim 22, further comprising an activity level sensor to detect an activity level of a patient, wherein the detector indicates myocardial ischemia based on the detected conduction time and the detected activity level.

42. A device comprising:

means for detecting cardiac conduction time; and

means for indicating myocardial ischemia based on the detected conduction time.

43. The device of claim 42, further comprising:

a first electrode for launching a stimulation wave front from a first electrode positioned proximate a first ventricular chamber; and

a second electrode for sensing a local cardiac depolarization at a second electrode positioned proximate a second ventricular chamber,

wherein the detecting means detects a time between launching the wave front and sensing the local cardiac depolarization.

44. The device of claim 43, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an epicardial electrode positioned on a surface of the second ventricular chamber.

45. The device of claim 43, wherein the first electrode includes an endocardial electrode positioned within the first ventricular chamber, and the second electrode includes an endocardial electrode positioned within the second ventricular chamber.

46. The device of claim 43, wherein the first ventricular chamber is the right ventricular chamber and the second ventricular chamber is the left ventricular chamber.

47. The device of claim 43, wherein the first ventricular chamber is the left ventricular chamber and the second ventricular chamber is the right ventricular chamber.

48. The device of claim 42, wherein the detecting means compares the detected conduction time to a threshold conduction time, and indicates ischemia when the detected conduction time exceeds the threshold conduction time.

49. The device of claim 42, wherein the detecting means adjusts the threshold conduction time based on a rate of change of the conduction time.

50. A method comprising:

launching a first stimulation wave front from a first ventricular chamber;

sensing a first local cardiac depolarization in a second ventricular chamber;

detecting a first time between launching the first wave front and sensing the first local cardiac depolarization;

launching a second stimulation wave front from the second ventricular chamber;

sensing a second local cardiac depolarization in the first ventricular chamber;

detecting a second time between launching the second wave front and sensing the second local cardiac depolarization; and

indicating myocardial ischemia based on the first time and the second time.

51. The method of claim 50, further comprising indicating myocardial ischemia based on a difference between the first time and second time.

52. A device comprising:

means for launching a first stimulation wave front from a first ventricular chamber;

means for sensing a first local cardiac depolarization in a second ventricular chamber;

means for detecting a first time between launching the first wave front and sensing the first local cardiac depolarization;

means for launching a second stimulation wave front from the second ventricular chamber;

means for sensing a second local cardiac depolarization in the first ventricular chamber;

means for detecting a second time between launching the second wave front and sensing the second local cardiac depolarization; and

means for indicating myocardial ischemia based on the first time and the second time.

53. The device of claim 52, further comprising means for indicating myocardial ischemia based on a difference between the first time and second time.

5

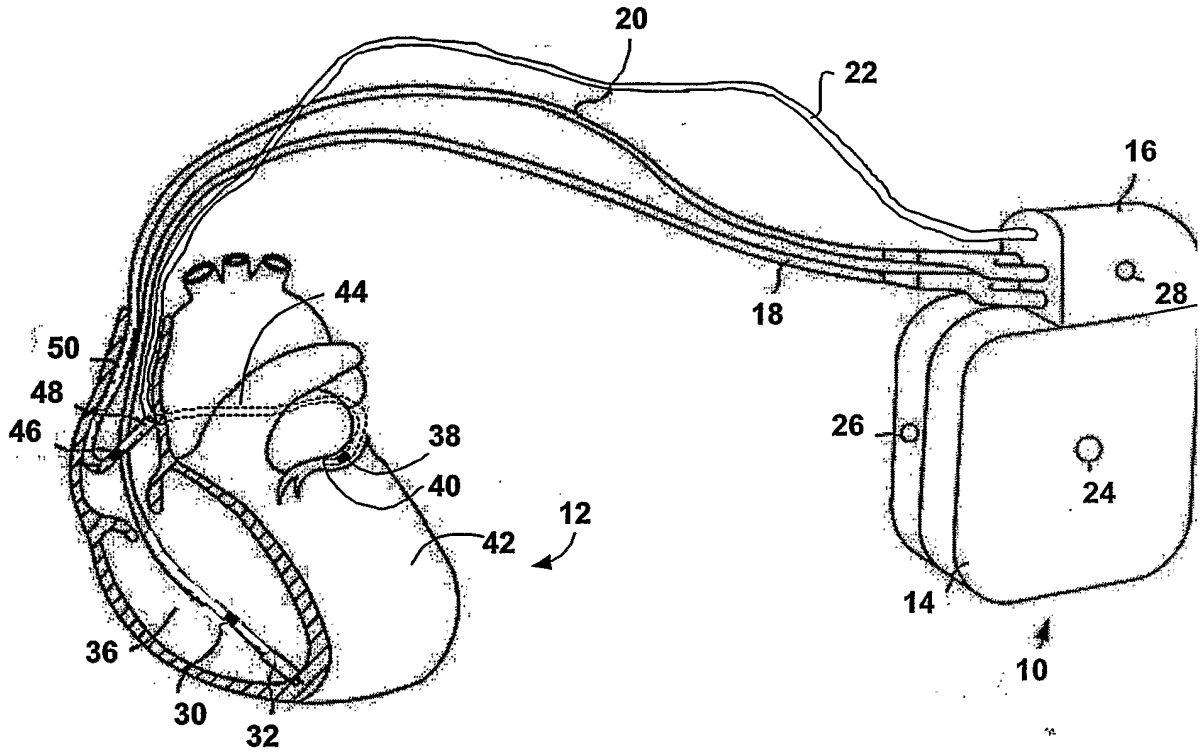

FIG. 1

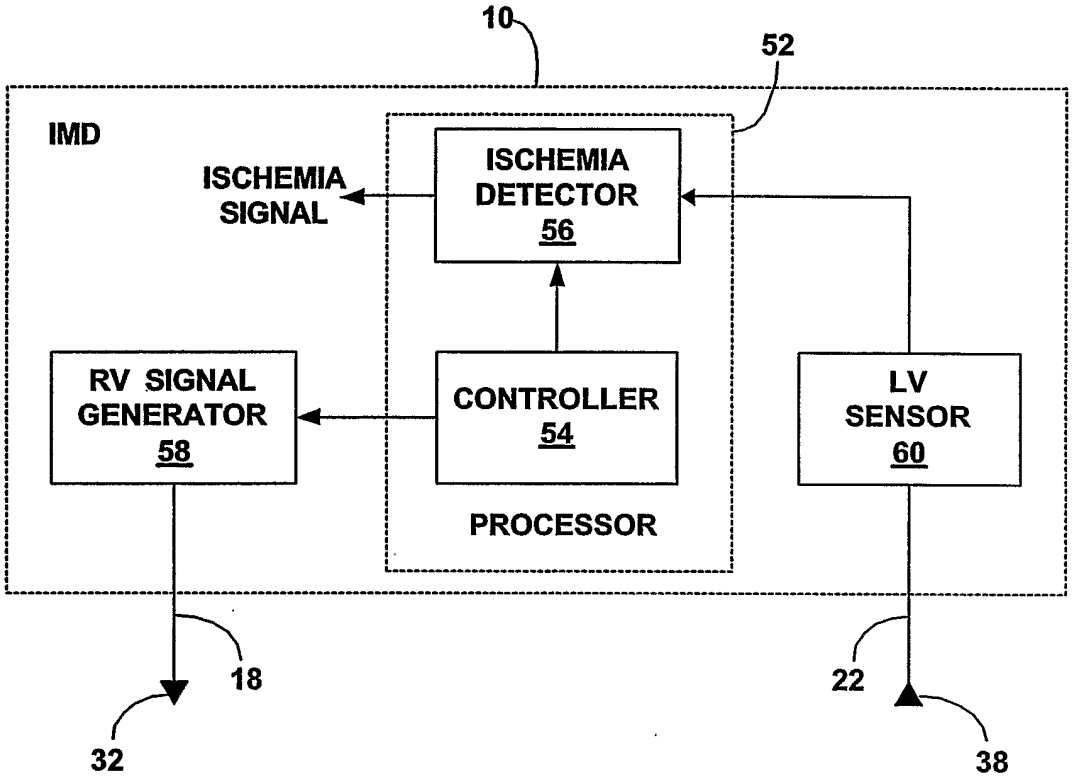
10
52
IMD
ISCHEMIA SIGNAL
ISCHEMIA DETECTOR 56
RV SIGNAL GENERATOR 58
CONTROLLER 54
LV SENSOR 60
PROCESSOR
18
22
32
38

FIG. 2

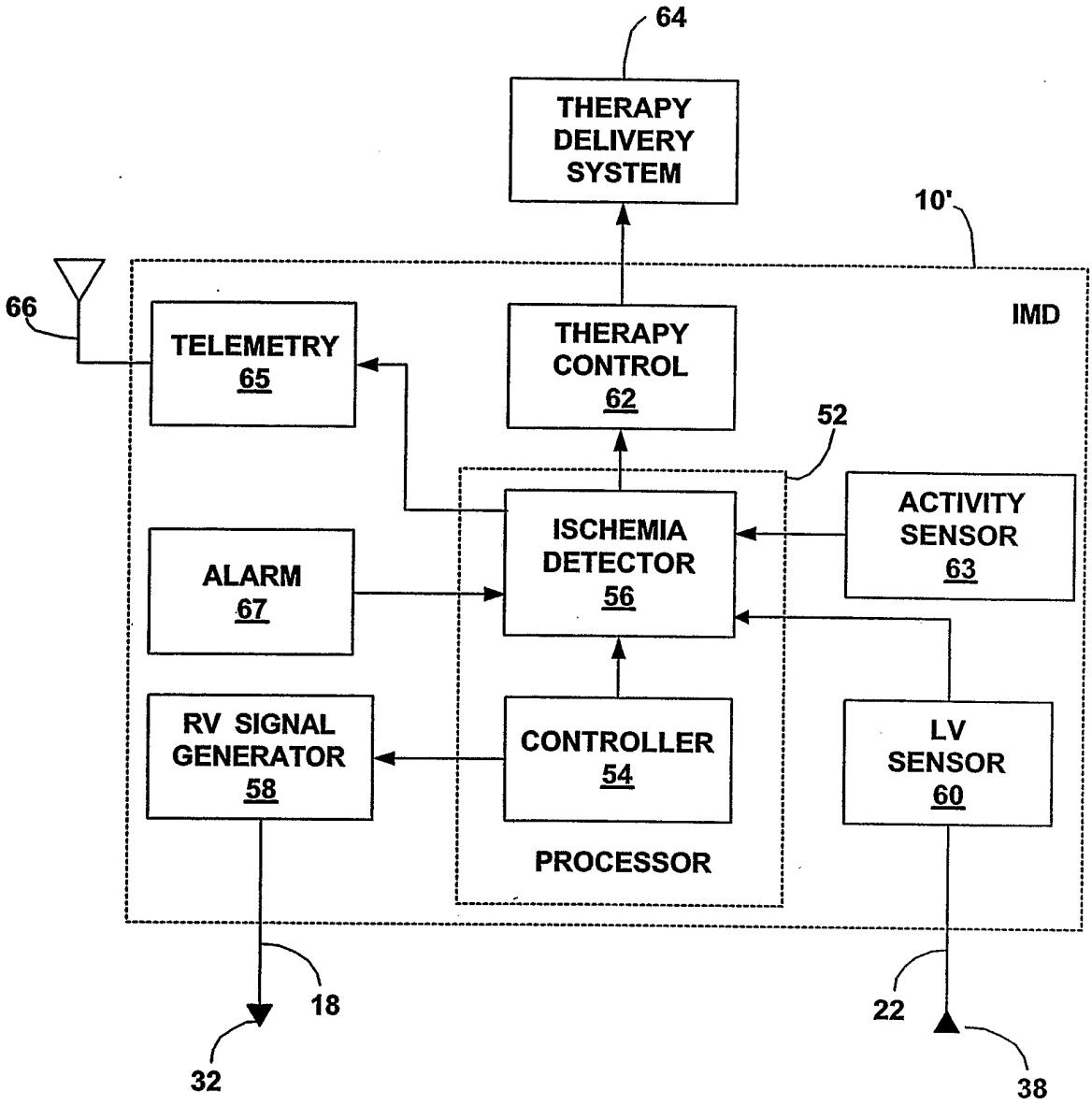
64
THERAPY DELIVERY SYSTEM
10'
IMD
66
TELEMETRY 65
THERAPY CONTROL 62
52
ACTIVITY SENSOR 63
ISCHEMIA DETECTOR 56
ALARM 67
RV SIGNAL GENERATOR 58
CONTROLLER 54
LV SENSOR 60
PROCESSOR
18
22
32
38

FIG. 3

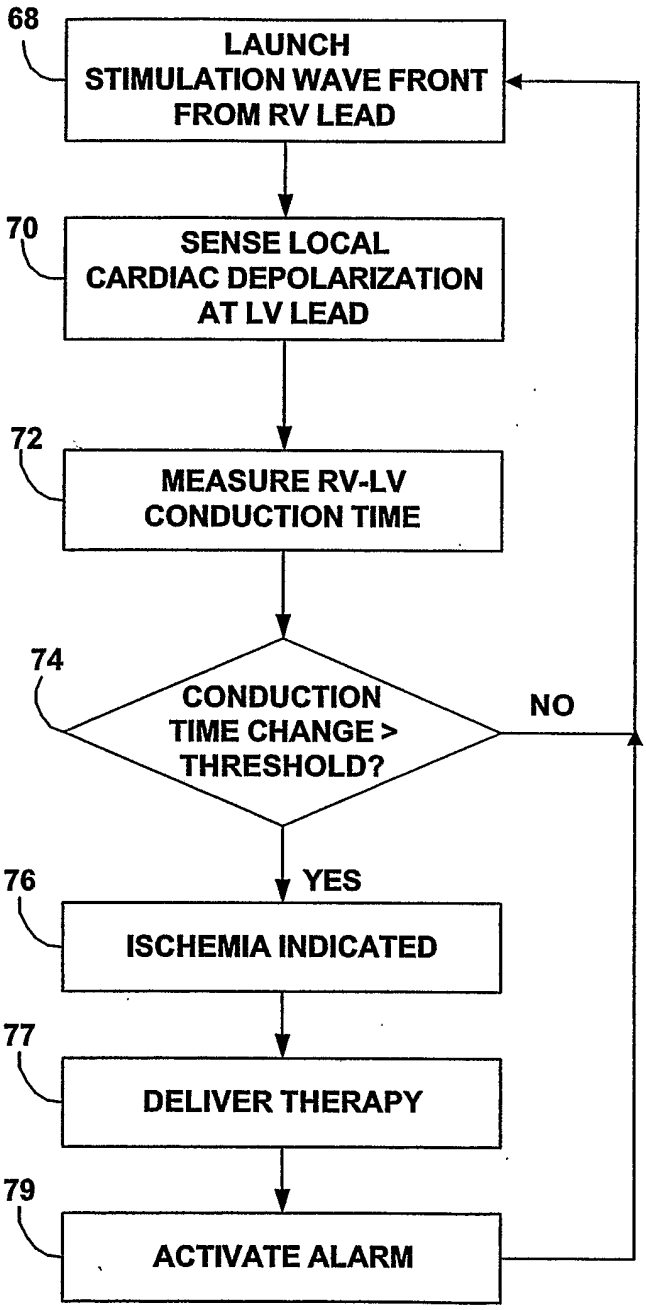
68
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
70
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
72
MEASURE RV-LV CONDUCTION TIME
74
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
76
ISCHEMIA INDICATED
77
DELIVER THERAPY
79
ACTIVATE ALARM

FIG. 4

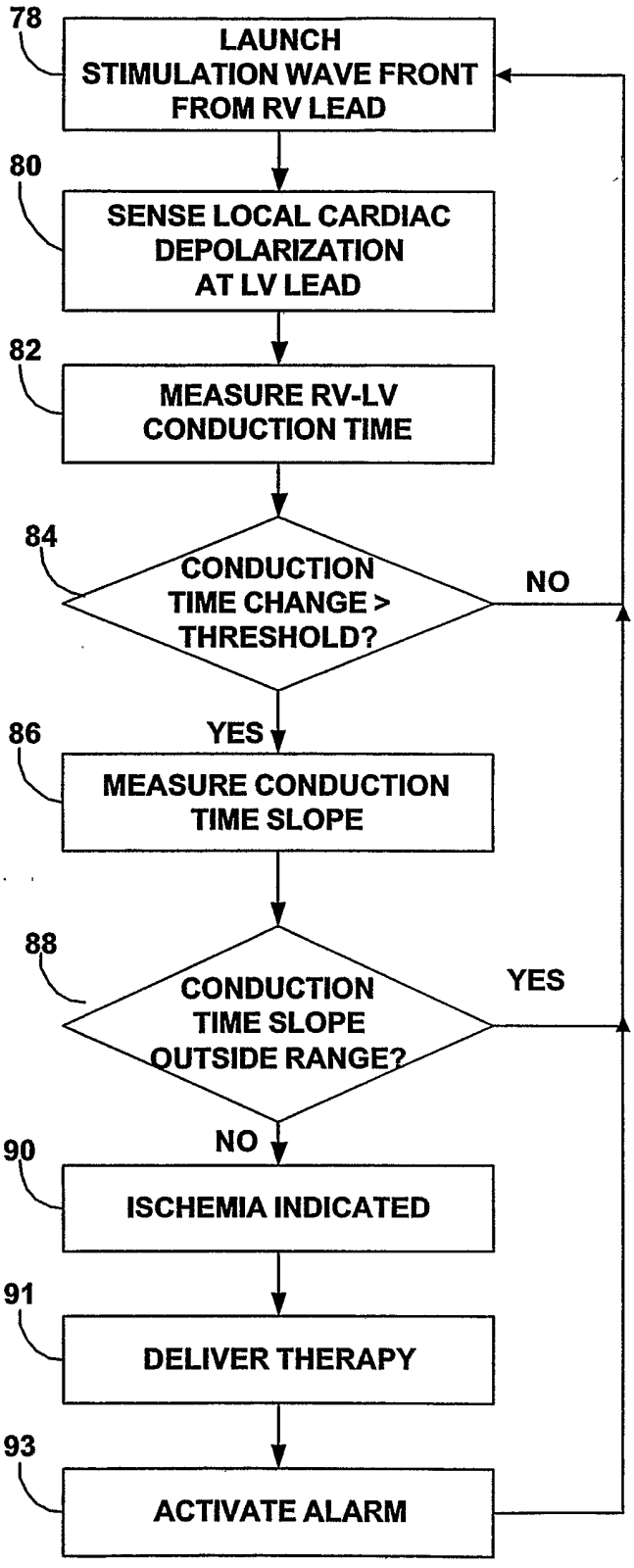
78
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
80
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
82
MEASURE RV-LV CONDUCTION TIME
84
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
86
MEASURE CONDUCTION TIME SLOPE
88
CONDUCTION TIME SLOPE OUTSIDE RANGE?
YES
NO
90
ISCHEMIA INDICATED
91
DELIVER THERAPY
93
ACTIVATE ALARM

FIG. 5

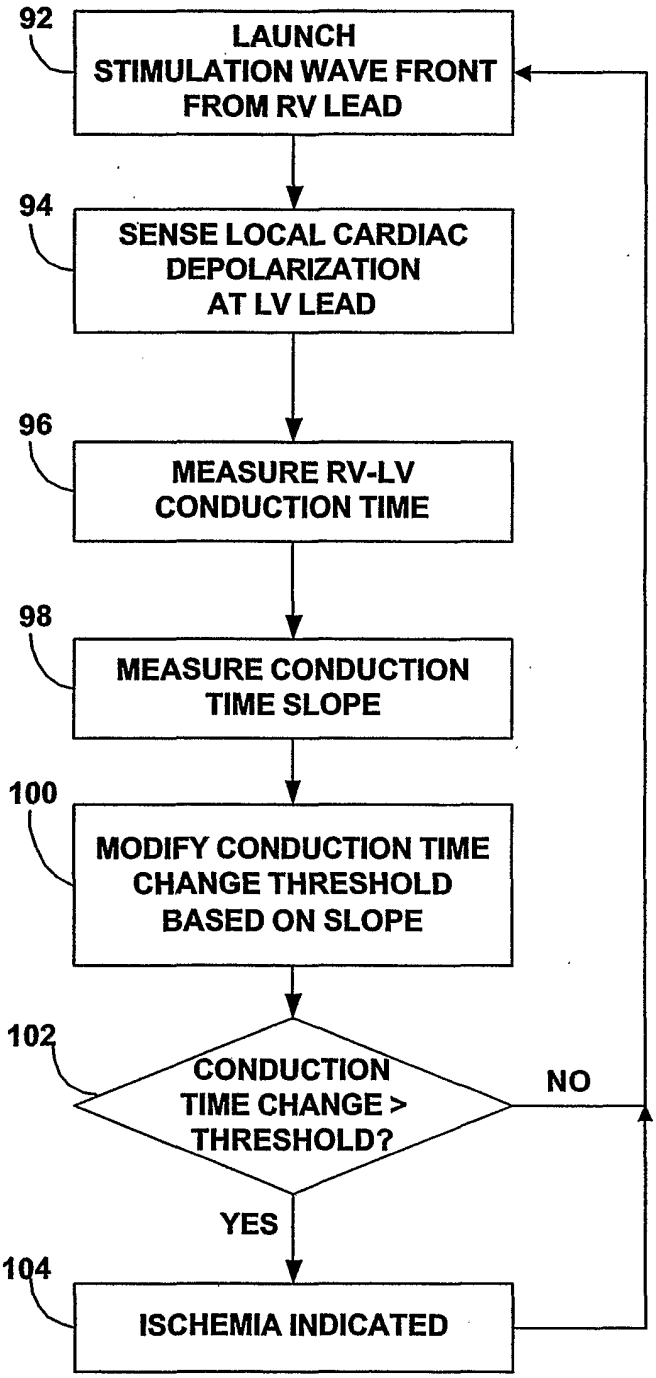
92
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
94
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
96
MEASURE RV-LV CONDUCTION TIME
98
MEASURE CONDUCTION TIME SLOPE
100
MODIFY CONDUCTION TIME CHANGE THRESHOLD BASED ON SLOPE
102
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
104
ISCHEMIA INDICATED

FIG. 6

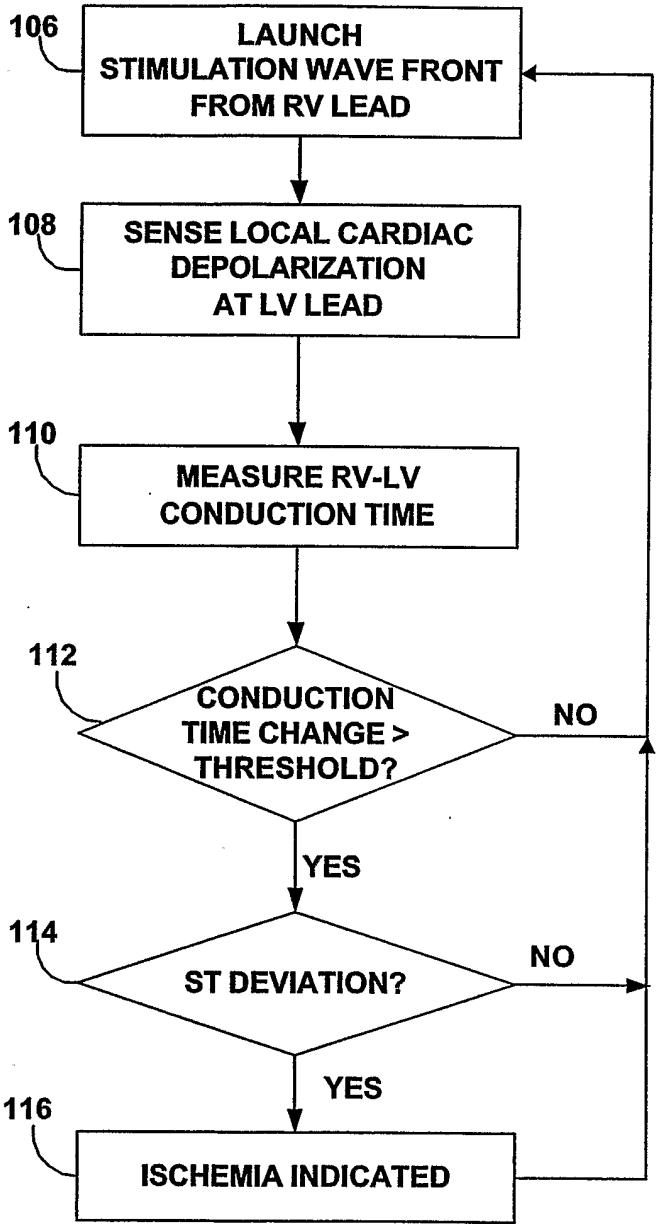
106
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
108
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
110
MEASURE RV-LV CONDUCTION TIME
112
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
114
ST DEVIATION?
NO
YES
116
ISCHEMIA INDICATED

FIG. 7

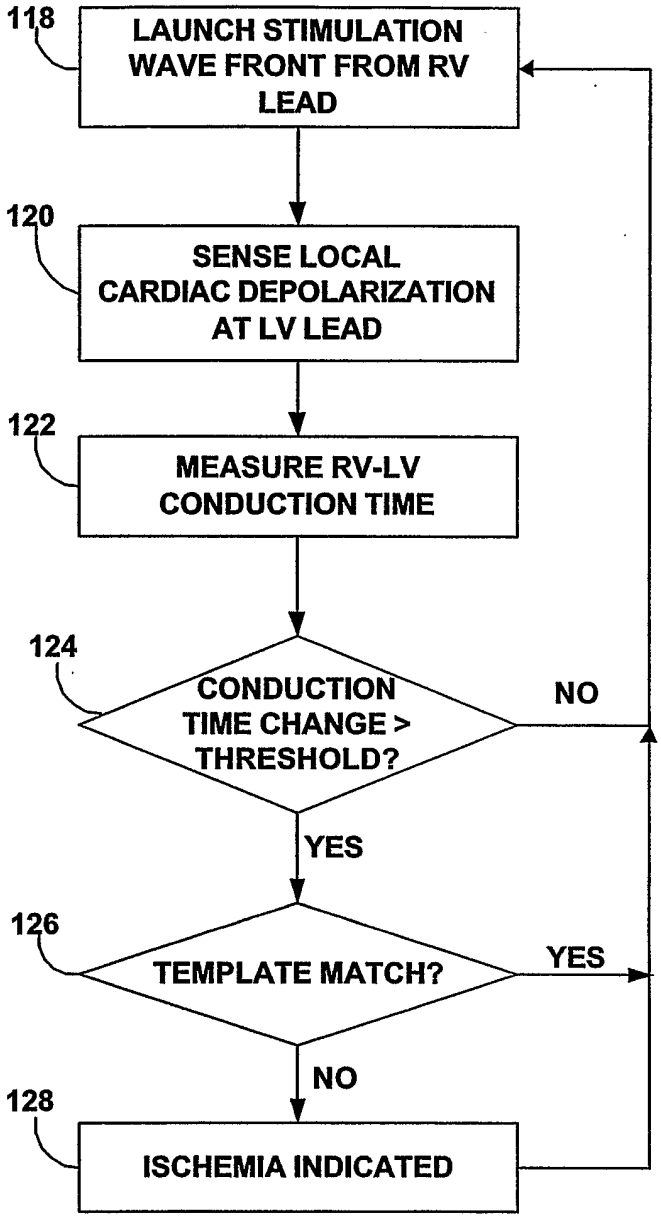
118
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
120
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
122
MEASURE RV-LV CONDUCTION TIME
124
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
126
TEMPLATE MATCH?
YES
NO
128
ISCHEMIA INDICATED

FIG. 8

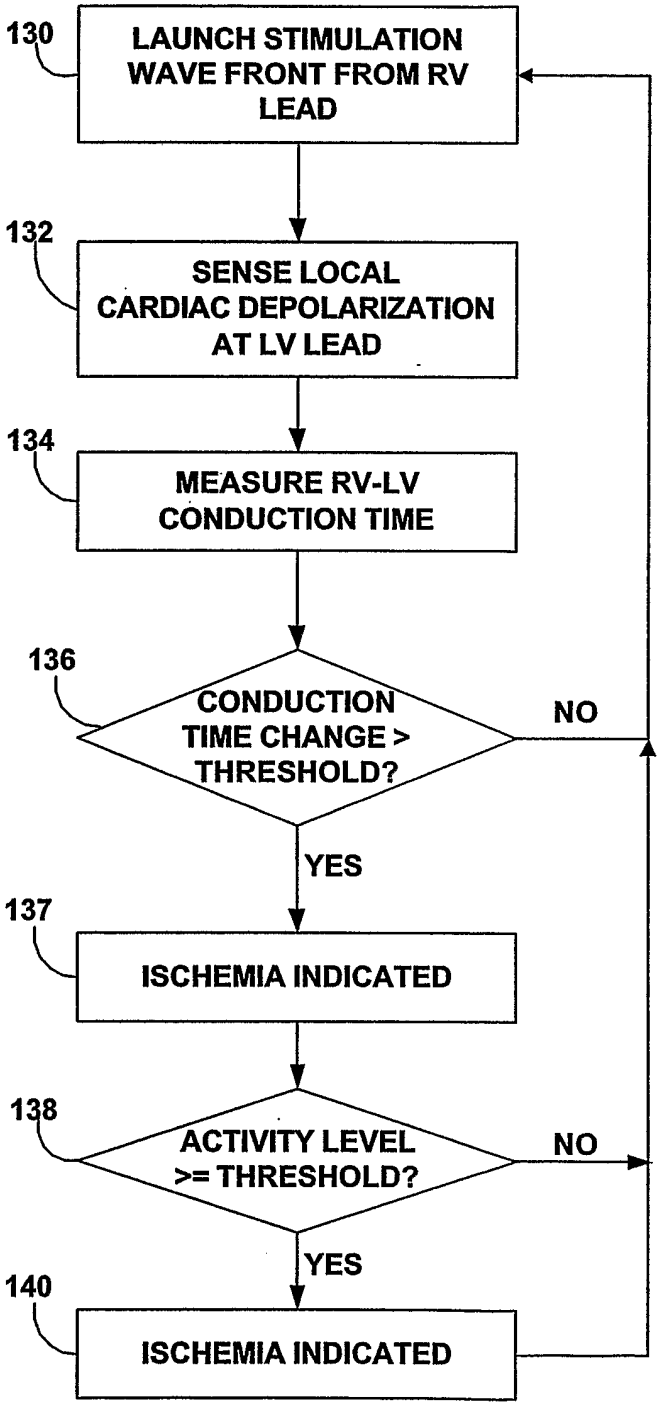
130
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
132
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
134
MEASURE RV-LV CONDUCTION TIME
136
CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
137
ISCHEMIA INDICATED
138
ACTIVITY LEVEL >= THRESHOLD?
NO
YES
140
ISCHEMIA INDICATED

FIG. 9

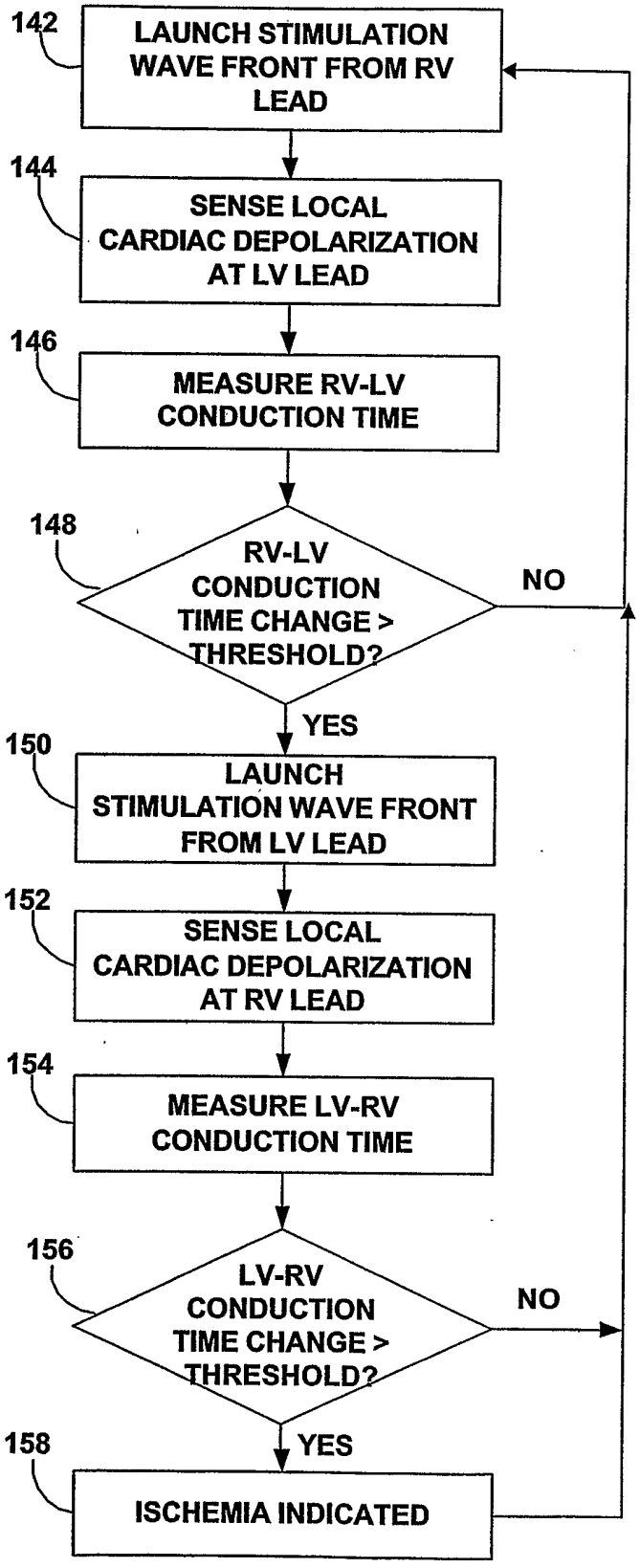
142
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
144
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
146
MEASURE RV-LV CONDUCTION TIME
148
RV-LV CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
150
LAUNCH STIMULATION WAVE FRONT FROM LV LEAD
152
SENSE LOCAL CARDIAC DEPOLARIZATION AT RV LEAD
154
MEASURE LV-RV CONDUCTION TIME
156
LV-RV CONDUCTION TIME CHANGE > THRESHOLD?
NO
YES
158
ISCHEMIA INDICATED

FIG. 10

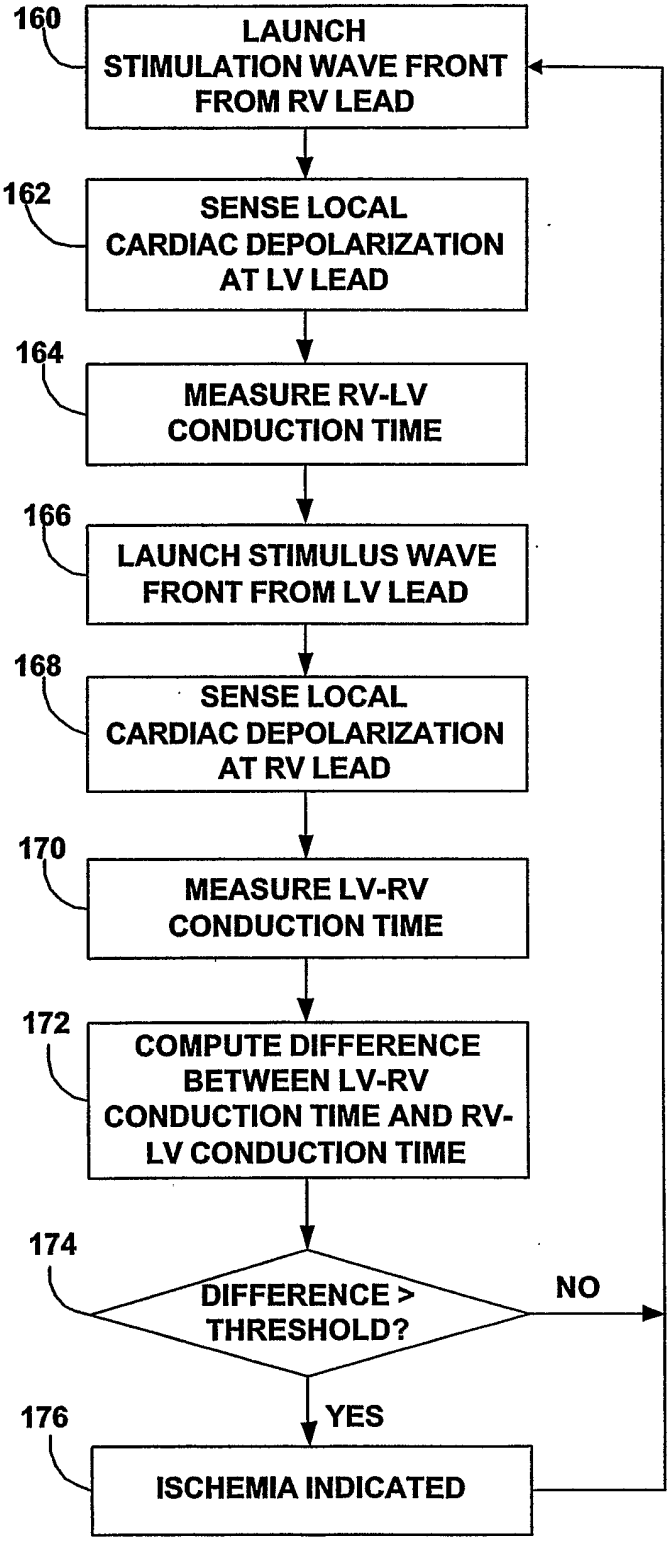
160
LAUNCH STIMULATION WAVE FRONT FROM RV LEAD
162
SENSE LOCAL CARDIAC DEPOLARIZATION AT LV LEAD
164
MEASURE RV-LV CONDUCTION TIME
166
LAUNCH STIMULUS WAVE FRONT FROM LV LEAD
168
SENSE LOCAL CARDIAC DEPOLARIZATION AT RV LEAD
170
MEASURE LV-RV CONDUCTION TIME
172
COMPUTE DIFFERENCE BETWEEN LV-RV CONDUCTION TIME AND RV-LV CONDUCTION TIME
174
DIFFERENCE > THRESHOLD?
NO
YES
176
ISCHEMIA INDICATED

FIG. 11

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/34586

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61N1/37 A61N1/365

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)
IPC 7 A61N A61B

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

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

EPO-Internal, WPI Data, PAJ, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 243 603 B1 (KENKNIGHT BRUCE H ET AL) 5 June 2001 (2001-06-05) column 1, line 14 -column 10, line 35	42-44, 46-48, 52,53
Y		22-25, 27-29, 32-37, 39-41,45
A		26,30, 31,38,49

X	US 5 243 981 A (HUDRLIK TERRENCE R) 14 September 1993 (1993-09-14) column 3, line 35-38	42
A		22-41, 43-49, 52,53

	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in 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 document 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
22 March 2004	30/03/2004

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, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Aronsson, F

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/34586

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2002/042578 A1 (STAROBIN JOSEPH M ET AL) 11 April 2002 (2002-04-11) paragraphs '0011!-'0050!,'0141!	22-24, 27-29, 32,33, 36,37, 39,40
Y	WO 97 24981 A (BIOSENSE ISRAEL LTD; FENSTER MAIER (IL); BEN HAIM SHLOMO (IL)) 17 July 1997 (1997-07-17) page 28, line 1,2; figure 6	25,45
Y	US 2002/016548 A1 (NELSON SHANNON ET AL) 7 February 2002 (2002-02-07) paragraph '0098!	35
Y	US 2002/072777 A1 (LU RICHARD) 13 June 2002 (2002-06-13) paragraphs '0010!-'0024!,'0035!,'0062!-'0064!	34,41

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/34586

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 1-21,50-51
because they relate to subject matter not required to be searched by this Authority, namely:

Claim 1-21: Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
Claim 50-51: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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