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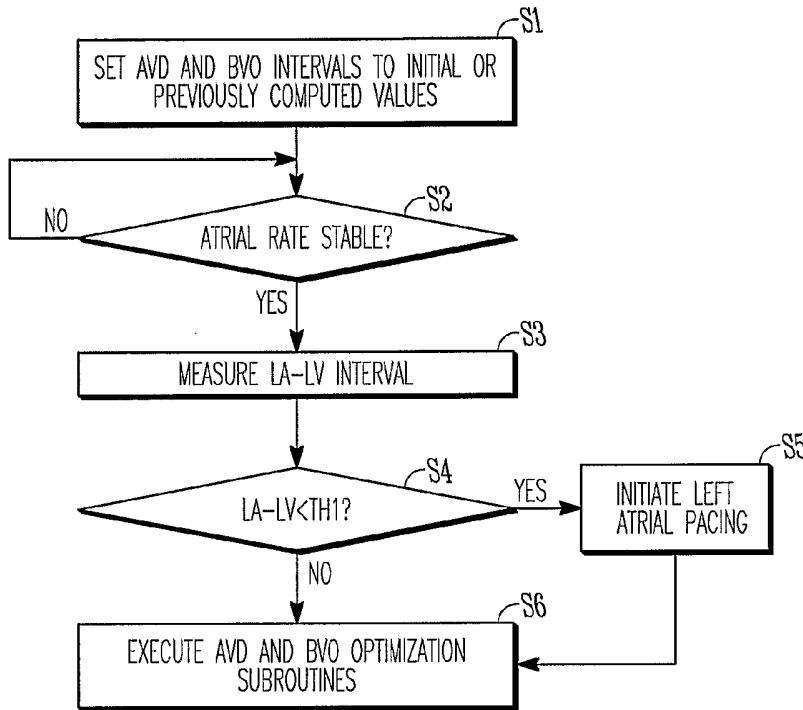
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(54) Title: APPARATUS FOR TREATMENT OF PROLONGED INTER-ATRIAL DELAY



(57) Abstract: A method and system for identifying and assessing inter-atrial conduction delays in patients is disclosed. Patients who are so identified and are also in need of ventricular resynchronization therapy may then be treated with left atrial pacing and ventricular resynchronization pacing. Certain patients may alternatively be treated with ventricular resynchronization therapy delivered with a conservatively selected atrio-ventricular delay interval and without left atrial pacing.

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## APPARATUS FOR TREATMENT OF PROLONGED INTER-ATRIAL DELAY

### CLAIM OF PRIORITY

5           Benefit of priority is hereby claimed to U.S. Patent Application Serial  
Number 11/113,809, filed on April 25, 2005, which application is herein  
incorporated by reference.

### RELATED APPLICATIONS

10           This application is a continuation-in-part of U.S. Patent Application  
Serial No. 10/920,698, filed on August 18, 2004, entitled "BIATRIAL PACING  
OPTIMIZATION FOR BIVENTRICULAR PACING", the disclosure of which  
is hereby incorporated by reference.

### FIELD OF THE INVENTION

15           This invention pertains to methods and apparatus for treating cardiac  
disease with electrical therapy.

### Background

20           Cardiac rhythm management devices are implantable devices that provide  
electrical stimulation to selected chambers of the heart in order to treat disorders  
of cardiac rhythm. A pacemaker, for example, is a cardiac rhythm management  
device that paces the heart with timed pacing pulses. The most common  
condition for which pacemakers are used is in the treatment of bradycardia,  
25           where the ventricular rate is too slow. Atrio-ventricular conduction defects (i.e.,  
AV block) that are permanent or intermittent and sick sinus syndrome represent  
the most common causes of bradycardia for which permanent pacing may be  
indicated. If functioning properly, the pacemaker makes up for the heart's  
inability to pace itself at an appropriate rhythm in order to meet metabolic  
30           demand by enforcing a minimum heart rate and/or artificially restoring AV  
conduction.

          Pacing therapy can also be used in the treatment of heart failure, which  
refers to a clinical syndrome in which an abnormality of cardiac function causes

a below normal cardiac output that can fall below a level adequate to meet the metabolic demand of peripheral tissues. When uncompensated, it usually presents as congestive heart failure due to the accompanying venous and pulmonary congestion. Heart failure can be due to a variety of etiologies with ischemic heart disease being the most common. It has been shown that some heart failure patients suffer from intraventricular and/or interventricular conduction defects (e.g., bundle branch blocks) such that their cardiac outputs can be increased by improving the synchronization of ventricular contractions with electrical stimulation. In order to treat these problems, implantable cardiac devices have been developed that provide appropriately timed electrical stimulation to one or more heart chambers in an attempt to improve the coordination of atrial and/or ventricular contractions, termed cardiac resynchronization therapy (CRT). Currently, a most common form of CRT applies stimulation pulses to both ventricles, either simultaneously or separated by a specified biventricular offset interval, and after a specified atrio-ventricular delay interval with respect to the detection of an intrinsic atrial contraction and/or an atrial pace.

Certain patients, in addition to having ventricular conduction problems, have prolonged inter-atrial conduction delays. A prolonged inter-atrial delay compromises the synchronization of atrial and ventricular contractions which can complicate the optimal delivery of CRT. It is this problem with which the present disclosure is primarily concerned.

#### SUMMARY

Patients with prolonged inter-atrial conduction delays exhibit delayed conduction of excitation from the right atrium to the left atrium. The delay may exist during intrinsic beats in which the excitation originates at the sino-atrial node in the right atrium, during an atrial paced beat in which the excitation originates at a right atrial pacing site, or both. The delayed contraction of the left atrium results in sub-optimal diastolic filling of the left ventricle during atrial systole and, hence, decreased cardiac output. Application of ventricular CRT in these patients in a conventional manner, where the left ventricle is pre-excited with pacing pulses and thus made to contract sooner during a cardiac cycle, may

worsen the asynchrony between the left atrium and the left ventricle and even cause the left ventricle to contract before the left atrium. Besides interfering with optimal delivery of CRT, such a reversed AV contraction sequence may have other adverse consequences.

5 One way by which an inter-atrial delay may be reduced is to resynchronize the atria by stimulating (i.e., pacing) the left atrium either instead of or in addition to stimulating the right atrium. Identifying the degree of inter-atrial delay which would have a negative impact on the effectiveness of CRT, however, is problematic. Another difficulty is assessing the inter-atrial delay in order to  
10 appropriately specify pacing parameters for delivering CRT with or without atrial resynchronization. Described below are methods and apparatus for identifying and assessing an inter-atrial delay by sensing electrical activity in the left atrium and left ventricle and measuring the delay between left atrial and left ventricular contractions, referred to as the LA-LV interval.

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#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a system diagram of exemplary hardware components for delivering cardiac resynchronization therapy.

Fig. 2 illustrates an exemplary algorithm for identifying and treating  
20 patients with prolonged inter-atrial conduction delays.

#### DETAILED DESCRIPTION

Described herein are a method and system for setting the pacing parameters and/or pacing configuration of a cardiac rhythm management device  
25 for delivering resynchronization pacing to the left ventricle (LV) and/or the right ventricle (RV) in order to compensate for ventricular conduction delays and improve the coordination of ventricular contractions. Another aspect of the disclosure involves the identification and assessment of inter-atrial conduction delays which can compromise the delivery of CRT by measuring the LA-LV  
30 interval. If the LA-LV interval is found to be less than a specified threshold, the patient may be treated with left atrial pacing to restore LA-LV synchrony. Alternatively, some patients may be treated with CRT using a conservative (i.e., long) AV delay interval.

### 1. Exemplary hardware platform

The following is a description of exemplary hardware components used for practicing the present invention. A block diagram of an implantable cardiac rhythm management device or pulse generator having multiple sensing and  
5 pacing channels is shown in Fig. 1. Pacing of the heart with an implanted device involves excitatory electrical stimulation of the heart by the delivery of pacing pulses to an electrode in electrical contact with the myocardium. The device is usually implanted subcutaneously on the patient's chest, and is connected to  
10 electrodes by leads threaded through the vessels of the upper venous system into the heart. An electrode can be incorporated into a sensing channel that generates an electrogram signal representing cardiac electrical activity at the electrode site and/or incorporated into a pacing channel for delivering pacing pulses to the site.

The controller of the device in Fig. 1 is made up of a microprocessor 10 communicating with a memory 12 via a bidirectional data bus, where the  
15 memory 12 typically comprises a ROM (read-only memory) and/or a RAM (random-access memory). The controller could be implemented by other types of logic circuitry (e.g., discrete components or programmable logic arrays) using a state machine type of design, but a microprocessor-based system is preferable. As used herein, the programming of a controller should be taken to refer to either  
20 discrete logic circuitry configured to perform particular functions or to the code executed by a microprocessor. The controller is capable of operating the pacemaker in a number of programmed modes where a programmed mode defines how pacing pulses are output in response to sensed events and expiration of time intervals. A telemetry interface 80 is provided for communicating with  
25 an external programmer 300. The external programmer is a computerized device with an associated display and input means that can interrogate the pacemaker and receive stored data as well as directly adjust the operating parameters of the pacemaker. As described below, in certain embodiments of a system for setting pacing parameters, the external programmer may be utilized for computing  
30 optimal pacing parameters from data received from the implantable device over the telemetry link which can then be set automatically or presented to a clinician in the form of recommendations.

The embodiment shown in Fig. 1 has four sensing/pacing channels, where a pacing channel is made up of a pulse generator connected to an electrode while a sensing channel is made up of the sense amplifier connected to an electrode. A MOS switching network 70 controlled by the microprocessor is used to switch the electrodes from the input of a sense amplifier to the output of a pulse generator. The switching network 70 also allows the sensing and pacing channels to be configured by the controller with different combinations of the available electrodes. The channels may be configured as either atrial or ventricular channels allowing the device to deliver conventional ventricular single-site pacing with or without atrial tracking, biventricular pacing, or multi-site pacing of a single chamber. In an example configuration, a left atrial (LA) sensing/pacing channel includes ring electrode 53a and tip electrode 53b of bipolar lead 53c, sense amplifier 51, pulse generator 52, and a channel interface 50, and a right atrial (RA) sensing/pacing channel includes ring electrode 43a and tip electrode 43b of bipolar lead 43c, sense amplifier 41, pulse generator 42, and a channel interface 40. A right ventricular (RV) sensing/pacing channel includes ring electrode 23a and tip electrode 23b of bipolar lead 23c, sense amplifier 21, pulse generator 22, and a channel interface 20, and a left ventricular (LV) sensing/pacing channel includes ring electrode 33a and tip electrode 33b of bipolar lead 33c, sense amplifier 31, pulse generator 32, and a channel interface 30. The channel interfaces communicate bi-directionally with a port of microprocessor 10 and include analog-to-digital converters for digitizing sensing signal inputs from the sensing amplifiers, registers that can be written to for adjusting the gain and threshold values of the sensing amplifiers, and registers for controlling the output of pacing pulses and/or changing the pacing pulse amplitude. In this embodiment, the device is equipped with bipolar leads that include two electrodes which are used for outputting a pacing pulse and/or sensing intrinsic activity. Other embodiments may employ unipolar leads with single electrodes for sensing and pacing. The switching network 70 may configure a channel for unipolar sensing or pacing by referencing an electrode of a unipolar or bipolar lead with the device housing or can 60.

The controller controls the overall operation of the device in accordance with programmed instructions stored in memory. The controller interprets

electrogram signals from the sensing channels and controls the delivery of paces in accordance with a pacing mode. An exertion level sensor 330 (e.g., an accelerometer, a minute ventilation sensor, or other sensor that measures a parameter related to metabolic demand) enables the controller to adapt the atrial and/or ventricular pacing rate in accordance with changes in the patient's physical activity, termed a rate-adaptive pacing mode. The sensing circuitry of the device generates atrial and ventricular electrogram signals from the voltages sensed by the electrodes of a particular channel. An electrogram is analogous to a surface EKG and indicates the time course and amplitude of cardiac depolarization and repolarization that occurs during either an intrinsic or paced beat. When an electrogram signal in an atrial or ventricular sensing channel exceeds a specified threshold, the controller detects an atrial or ventricular sense, respectively, which pacing algorithms may employ to trigger or inhibit pacing.

In one embodiment, the exertion level sensor is a minute ventilation sensor which includes an exciter and an impedance measuring circuit. The exciter supplies excitation current of a specified amplitude (e.g., as a pulse waveform with constant amplitude) to excitation electrodes that are disposed in the thorax. Voltage sense electrodes are disposed in a selected region of the thorax so that the potential difference between the electrodes while excitation current is supplied is representative of the transthoracic impedance between the voltage sense electrodes. The conductive housing or can may be used as one of the voltage sense electrodes. The impedance measuring circuitry processes the voltage sense signal from the voltage sense electrodes to derive the impedance signal. Further processing of the impedance signal allows the derivation of signal representing respiratory activity and/or cardiac blood volume, depending upon the location the voltage sense electrodes in the thorax or cardiac anatomy. (See, e.g., U.S. Patent Nos. 5,190,035 and 6,161,042, assigned to the assignee of the present invention and hereby incorporated by reference.) If the impedance signal is filtered to remove the respiratory component, the result is a signal that is representative of blood volume in the heart at any point in time, thus allowing the computation of stroke volume and, when combined with heart rate, computation of cardiac output.



## 2. Cardiac resynchronization pacing therapy

Cardiac resynchronization therapy is most conveniently delivered in conjunction with a bradycardia pacing mode. Bradycardia pacing modes refer to pacing algorithms used to pace the atria and/or ventricles in a manner that enforces a certain minimum heart rate. Because of the risk of inducing an arrhythmia with asynchronous pacing, most pacemakers for treating bradycardia are programmed to operate synchronously in a so-called demand mode where sensed cardiac events occurring within a defined interval either trigger or inhibit a pacing pulse. Inhibited demand pacing modes utilize escape intervals to control pacing in accordance with sensed intrinsic activity. In an inhibited demand mode, a pacing pulse is delivered to a heart chamber during a cardiac cycle only after expiration of a defined escape interval during which no intrinsic beat by the chamber is detected. For example, a ventricular escape interval for pacing the ventricles can be defined between ventricular events, referred to as the cardiac cycle (CC) interval with its inverse being the lower rate limit or LRL. The CC interval is restarted with each ventricular sense or pace. In atrial tracking and AV sequential pacing modes, another ventricular escape interval is defined between atrial and ventricular events, referred to as the atrio-ventricular pacing delay interval or AVD, where a ventricular pacing pulse is delivered upon expiration of the atrio-ventricular pacing delay interval if no ventricular sense occurs before. In an atrial tracking mode, the atrio-ventricular pacing delay interval is triggered by an atrial sense and stopped by a ventricular sense or pace. An atrial escape interval can also be defined for pacing the atria either alone or in addition to pacing the ventricles. In an AV sequential pacing mode, the atrio-ventricular delay interval is triggered by an atrial pace and stopped by a ventricular sense or pace. Atrial tracking and AV sequential pacing are commonly combined so that an AVD starts with either an atrial pace or sense. When used in CRT, the AVD may be the same or different in the cases of atrial tracking and AV sequential pacing.

As described above, cardiac resynchronization therapy is pacing stimulation applied to one or more heart chambers in a manner that compensates for conduction delays. Ventricular resynchronization pacing is useful in treating heart failure in patients with interventricular or intraventricular conduction

defects because, although not directly inotropic, resynchronization results in a more coordinated contraction of the ventricles with improved pumping efficiency and increased cardiac output. Ventricular resynchronization can be achieved in certain patients by pacing at a single unconventional site, such as the

5 left ventricle instead of the right ventricle in patients with left ventricular conduction defects. Resynchronization pacing may also involve biventricular pacing with the paces to right and left ventricles delivered either simultaneously or sequentially, with the interval between the paces termed the biventricular offset (BVO) interval (also sometimes referred to as the LV offset (LVO)

10 interval or VV delay). The offset interval may be zero in order to pace both ventricles simultaneously, or non-zero in order to pace the left and right ventricles sequentially. As the term is used herein, a negative BVO refers to pacing the left ventricle before the right, while a positive BVO refers to pacing the right ventricle first. In an example biventricular resynchronization pacing

15 mode, right atrial paces and senses trigger an AVD interval which upon expiration results in a pace to one of the ventricles and which is stopped by a right ventricular sense. The contralateral ventricular pace is delivered at the specified BVO interval with respect to expiration of the AVD interval.

Cardiac resynchronization therapy is most commonly applied in the

20 treatment of patients with heart failure due to left ventricular dysfunction which is either caused by or contributed to by left ventricular conduction abnormalities. In such patients, the left ventricle or parts of the left ventricle contract later than normal during systole which thereby impairs pumping efficiency. This can occur during intrinsic beats and during paced beats when only the right ventricle is

25 paced. In order to resynchronize ventricular contractions in such patients, pacing therapy is applied such that the left ventricle or a portion of the left ventricle is pre-excited relative to when it would become depolarized during an intrinsic or right ventricle-only paced beat. Optimal pre-excitation of the left ventricle in a given patient may be obtained with biventricular pacing or with left ventricular-

30 only pacing. Although not as common, some patients have a right ventricular conduction deficit such as right bundle branch block and require pre-excitation of the right ventricle in order achieve synchronization of their ventricular contractions.

### 3. CRT pacing configuration and mode for patients with atrial conduction deficit

In certain patients, an atrial conduction deficit exists such that left atrio-ventricular synchrony does not occur during intrinsic beats even if the intrinsic atrio-ventricular interval as measured from a right atrial sense to a right ventricular sense is normal. This is exasperated by right atrial pacing and the common location of right atrial appendage pacing. Measurement of the inter-atrial conduction times has demonstrated an increase when right atrial pacing as compared with conduction of an intrinsic atrial event. Additionally there may be an abnormal conduction delay between atria in up to 20 % of CRT patients. A primary aspect of the present disclosure involves determining if such an atrial conduction deficit exists and adjusting pacing parameters accordingly. One way of determining whether an atrial conduction deficit exists is to measure the interval between a right atrial sense or pace and a left atrial sense, referred to as the RA-LA interval, as described in co-pending application Serial No. 10/920,698, entitled "BIATRIAL PACING OPTIMIZATION FOR BIVENTRICULAR PACING". A parameter which may more directly reflect the degree of asynchrony between the left atrium and left ventricle, however, is the interval between a left atrial contraction and a left ventricular contraction, referred to as the LA-LV interval.

Measurement of the LA-LV interval may be implemented by an implantable device for delivering CRT such as illustrated in Fig. 1 which has sensing/pacing channels for both atria and both ventricles. In one embodiment, after standard placement of the RA lead, an LA lead/catheter is placed either directly in the left atrium or at the upper inter-atrial septum (e.g., Backman's bundle region). The LV lead is then placed using a standard approach (e.g., in the coronary sinus or a cardiac vein). The LA-LV interval may then be measured as the time between senses generated by the electrodes of the LA lead/catheter and the LV lead during sinus rhythm and/or during pacing of the right atrium at one or more particular rates. In an alternative embodiment, a single coronary sinus (CS) lead with two sets of electrodes may be used. In this configuration, one or more electrodes will be at the distal side of the lead to sense or pace the LV, while there are one or more electrodes in the middle of the lead such that

they will be disposed near the opening of the CS to sense or pace the left atrium. The LA-LV delay interval may then be measured as the time between senses generated by the distal and middle electrodes during sinus rhythm and/or during pacing of the right atrium at one or more particular rates. In still another

5 embodiment, the LA-LV interval is measured during the LV lead implantation procedure. In this technique, the LV lead is temporarily positioned at the mid-portion of the coronary sinus while the lead is being implanted in order to sense the left atrium. The RA lead is also positioned. Using either the implantable device or an external device equipped with multiple sensing channels, the time

10 interval between an RA sense or pace and an LA sense from the temporarily positioned LV is measured as the RA-LA interval. The LV lead is then further advanced through the CS to its final desired position for sensing the LV. The RA-LV delay is next measured as the interval between an RA sense and an LV sense. The LA-LV delay interval may then be computed as:

15

$$\text{LA-LV delay} = \text{RA-LV delay} - \text{RA-LA delay}$$

In one embodiment, the implantable device is configured to deliver biventricular pacing in a manner specified by AVD and BVO intervals. An

20 additional pacing parameter is also provided for pacing the left atrium, if necessary, referred to as the AAL interval, which is an escape interval triggered by a right atrial event and results in a left atrial pace upon expiration. If the measured LA-LV interval is less than a specified threshold amount, it can be surmised that a conduction deficit exists between the right and left atria, causing

25 asynchrony between the left atrium and left ventricle. The device can therefore be configured to pace the left atrium at an AAL interval (where a zero AAL interval paces both atria simultaneously) which synchronizes left atrial and left ventricular contractions. In an alternate embodiment, the timing for left atrial pacing may be based upon left ventricular events. This involves pacing the left

30 atrium at a specified offset interval VAL with respect to the time at which a left ventricular pace is delivered. A negative VAL interval thus delivers a pace to the left atrium before the left ventricle is paced and may be used in non-atrial triggered and non-AV sequential modes as well atrial triggered and AV

sequential pacing modes. In another embodiment, left atrial pacing can be based upon both right atrial and left ventricular events so that both AAL and VAL intervals are defined.

5 4. Optimal adjustment of pre-excitation timing parameters

Once a particular resynchronization pacing configuration and mode is selected for a patient, pacing parameters affecting the manner and extent to which pre-excitation is applied must be specified. For optimum hemodynamic performance, it is desirable to deliver ventricular pacing, whether for  
10 resynchronization pacing or conventional bradycardia pacing, in an atrial tracking and/or AV sequential pacing mode in order to maintain the function of the atria in pre-loading the ventricles (sometimes referred to as atrio-ventricular synchrony). Since the objective of CRT is to improve a patient's cardiac pumping function, it is therefore normally delivered in an atrial-tracking and/or  
15 AV sequential mode and requires specification of AVD and BVO intervals which, ideally, result in the ventricles being synchronized during systole after being optimally preloaded during atrial systole. That is, both optimal interventricular synchrony and optimal atrio-ventricular synchrony are achieved. As the term is used herein for biventricular pacing, the AVD interval refers to the  
20 interval between an atrial event (i.e., a pace or sense in one of the atria, usually the right atrium) and the first ventricular pace which pre-excites one of the ventricles. The AVD interval may be the same or different depending upon whether it is initiated by an atrial sense or pace (i.e., in atrial tracking and AV sequential pacing modes, respectively), The pacing instant for the non-pre-  
25 excited ventricle is specified by the BVO interval so that it is paced at an interval  $AVD + BVO$  after the atrial event. It should be appreciated that specifying AVD and BVO intervals is the same as specifying a separate AVD interval for each ventricle, designated as AVDR for the right ventricle and AVDL for the left ventricle. In patients with intact and normally functioning AV conduction  
30 pathways to the non-pre-excited ventricle, the non-pre-excited ventricle will be paced, if at all, close to the time at which that ventricle is intrinsically activated in order to achieve optimal preloading. In patients with normal AV conduction to the non-pre-excited ventricle, the optimal AVD and BVO intervals are thus

related to both the intrinsic atrio-ventricular interval and the amount of pre-excitation needed for one ventricle relative to the other (i.e., the extent of the ventricular conduction deficit).

In order to optimally specify the AVD and BVO parameters for a particular patient, clinical hemodynamic testing may be performed after  
5 implantation where the parameters are varied as cardiac function is assessed. For example, a patient may be given resynchronization stimulation while varying pre-excitation timing parameters in order to determine the values of the parameters that result in maximum cardiac performance, as determined by  
10 measuring a parameter reflective of cardiac function such as maximum left ventricular pressure change (dP/dt), arterial pulse pressure, or measurements of cardiac output. Determining optimal pacing parameters for an individual patient by clinical hemodynamic testing, however, is difficult and costly. It would be advantageous if such optimal pacing parameters could be determined from data  
15 collected by the implantable device. In one approach, a variable related to cardiac output, such as transthoracic impedance, is used to compute optimum values of resynchronization pacing parameters. In one embodiment, this allows dynamic changes in device behavior to occur in response to the patient's condition through cardiac remodeling, medication changes and physiologic  
20 changes.

In an example embodiment, an implantable cardiac resynchronization device is configured to deliver biventricular pacing in an atrial tracking or AV sequential pacing mode with a specified atrio-ventricular (AVD) interval. The AVD interval (and/or BVO interval) is then varied while measuring a variable  
25 related to cardiac output such as transthoracic impedance or intracardiac ultrasound (either external or integral to the device system). The AVD interval can then be set to a value which maximizes the variable related to cardiac output. The AVD interval may be varied, for example, using a binary search algorithm to derive the value of the AVD interval which maximizes the variable related to  
30 cardiac output. As described above, an inter-atrial conduction delay which is greater than normal may make it necessary to pace the left atrium in order to achieve optimal synchronization of the left atrium and the left ventricle. The LA-LV delay interval is therefore measured by the techniques described above,

with left atrial pacing initiated if the LA-LV interval exceeds a specified threshold Th1. Additionally following the optimization of the AV delay for maximum cardiac output, the LA-LV timing may be optimized in relationship to maximum cardiac output.

5           The techniques for setting resynchronization pacing parameters as described herein may be implemented in a number of different ways. In one implementation, a system for setting the pacing parameters includes an external programmer. In an example embodiment, a parameter related to cardiac output is measured by an implantable cardiac resynchronization device equipped with a  
10   transthoracic impedance sensor and transmitted to the external programmer via a wireless telemetry link. Either automatically or under the direction of the external programmer, the implantable device then varies the AVD and/or BVO intervals while measuring the variable related to cardiac output and measures the LA-LV interval during an intrinsic and/or right atrial paced cycle. In an  
15   automated system, the external programmer then automatically programs the implantable device with the computed optimum pacing parameter values, while in a semi-automated system the external programmer presents the computed optimum values to a clinician in the form of a recommendation. An automated system may also be made up of the implantable device alone which collects  
20   cardiac output data while varying the AVD and BVO intervals, measures the LA-LV interval and initiates left atrial pacing if necessary, determines the optimum parameter values which maximize cardiac output, and then sets the parameters accordingly. In another embodiment, which may be referred to as a manual system, the external programmer presents the collected cardiac output data and  
25   corresponding AVD and BVO intervals, as well as the LA-LV interval to a clinician for evaluation. Unless otherwise specified, references to a system for computing or setting pacing parameters throughout this document should be taken to include any of the automated, semi-automated, or manual systems just described. Another manual system could incorporate manual measurement of CO  
30   with external cardiac ultrasound while the device or external programmer optimizes the pacing parameters in a step like fashion.

### 5. Exemplary algorithm for computing pacing parameters and setting pacing configuration

Fig. 2 illustrates an exemplary algorithm for computing the optimal pacing parameters of an implantable cardiac rhythm management device for delivering biventricular pacing. The algorithm may be partially or wholly implemented as code executed by the device controller or by an external programmer. The implantable device may be equipped with sensing and pacing channels for both ventricles and both atria as shown in Fig. 1. The device is programmed to deliver right and left ventricular paces separated by specified biventricular offset interval BVO and in an atrial tracking or AV sequential mode so that the ventricular paces are delivered at an atrio-ventricular delay interval AVD following an atrial event. At step S1, the AVD and BVO intervals are either set to nominal initial values or are as set by a previous execution of the algorithm. At step S2, the atrial rate (either paced or intrinsic) is measured and tested for stability. If the atrial rate is stable, the LA-LV interval is measured at step S3. The measured LA-LV interval may be either a single measurement or an average of LA-LV interval measurements taken over a number of beats. At step S4, the LA-LV interval is compared with a specified threshold value Th1. If the LA-LV interval is less than Th1, left atrial pacing is initiated at step S5. This will initiate left atrial contraction preceding the left ventricular event mimicking the normal physiologic events. Since this is not a 'normal' heart, minor timing variations may improve cardiac efficiency. For example in the enlarged heart and pathologically damaged left side, left atrial contraction may need to precede the left ventricular event by a greater amount than in the 'normal' healthy heart to allow full LA contraction and atrial augmentation of left ventricular filling. The algorithm then proceeds to step S6 where optimization subroutines are performed for the AVD and BVO intervals. During an optimization subroutine, the interval (either the AVD or BVO) is varied while a variable related to cardiac output is measured, with the optimum value of the interval selected as the interval value which results in maximum cardiac output.

Alternatively, if the LA-LV interval is less than Th1 and if the patient does not have intact native AV conduction allowing the use of a longer than normal AVD interval, CRT may be delivered without left atrial pacing and with



a conservative AVD value which pre-excites the left ventricle later than normal. If the patient has normal AV conduction to the right ventricle, the optimum AVD value will normally be very close to the intrinsic atrio-ventricular interval and cannot be lengthened beyond it in order to compensate for an inter-atrial  
5 conduction delay. If on the other hand, the patient does not have intact native AV conduction such as complete AV block or a prolonged AV delay, it may be desirable to compensate for a prolonged inter-atrial delay with conservative AVD value rather than pacing the left atrium. In this approach, a long AVD value is used to pre-excite the left ventricle later than would be considered  
10 normal so as to maintain LA-LV synchrony even with the delayed LA contraction. A long AVD value may also be found with a cardiac output maximizing algorithm for computing an optimal AVD value. The AVD optimization subroutine, by finding the AVD value which produces maximum cardiac output, will give an AVD interval which is longer than the optimum  
15 AVD interval it would find if there were no inter-atrial delay. The optimization subroutine effectively adds the inter-atrial delay to the optimum AVD interval which would be found if there were no inter-atrial delay since it is synchrony between the left atria and ventricle that is most responsible for maximizing cardiac output.

20 In another embodiment, after finding the optimum AVD as measured by cardiac output or other cardiac function, the algorithm may adjust an initial RA to LA timing (perhaps based on averaged measured patient values) through a step up/step down algorithm applied to either an AAL or VAL interval used to pace the left atrium, thus optimizing the LA-LV interval and additionally  
25 maximizing the cardiac output. The algorithm may also follow optimization of the AVD and LA-LV intervals with re-optimization of the AVD interval to confirm that it was not negatively affected by changing the inter-atrial timing.

The algorithm illustrated in Fig. 2 may be performed periodically or upon command from an external programmer. In some situations, it may be desirable  
30 for the patient to remain in a steady state during optimization of pacing parameters. Such an optimization procedure may be performed, for example, in a physician's facility or automatically by the implantable device while the patient is sleeping. Optimization of pacing parameters may also be performed during

exercise (treadmill testing) since it is expected that these values will change with heart rate. This would allow the computation of dynamic optimum AV delays and inter-atrial timing as occurs in the normal physiologic heart. In this manner optimum values for the AVD, BVO, and left atrial pacing intervals may be  
5 computed for a plurality of heart rate ranges. For example, the algorithm may first determine which of a plurality of heart rate ranges corresponds to the current measured atrial rate. Optimum AVD, BVO, and left atrial pacing intervals are then computed as described above for that particular heart rate range. The device controller is then programmed to use those optimum AVD, BVO, and/or left  
10 atrial pacing interval values which have been computed for the current atrial rate.

Although the invention has been described in conjunction with the foregoing specific embodiments, many alternatives, variations, and modifications will be apparent to those of ordinary skill in the art. Other such alternatives, variations, and modifications are intended to fall within the scope of the  
15 following appended claims.

What is claimed is:

1. A method for delivering cardiac resynchronization therapy to a patient, comprising:
  - 5 measuring the interval from a left atrial sense to a left ventricular sense during an intrinsic or right atrial paced cardiac cycle, designated as the LA-LV interval;
  - comparing the LA-LV interval to a specified threshold Th1 and identifying the patient as having a prolonged inter-atrial delay if the LA-LV
  - 10 interval is less than the threshold Th1; and,
  - adjusting the manner in which the cardiac resynchronization therapy is delivered to compensate for the prolonged inter-atrial delay.
2. The method of claim 1 wherein the cardiac resynchronization therapy is
- 15 delivered as biventricular pacing with left atrial pacing to the patient if the LA-LV interval is less than the threshold Th1.
3. The method of claim 1 wherein the cardiac resynchronization therapy is delivered as biventricular pacing in an atrial tracking or AV sequential pacing
- 20 mode with a specified atrio-ventricular (AVD) interval, and further wherein the AVD interval is selected to be long enough to maintain adequate left atrial-left ventricular synchrony if the LA-LV interval is less than the threshold Th1.
4. The method of claim 3 further comprising:
  - 25 varying the AVD interval while measuring a variable related to cardiac output; and,
  - computing the optimum AVD interval as the value of the AVD interval which maximizes the variable related to cardiac output.
- 30 5. The method of claim 4 wherein the variable related to cardiac output is transthoracic impedance.

6. The method of claim 2 wherein the left atrium is paced at a specified atrial-atrial delay (AAL) interval following a right atrial sense or pace.
7. The method of claim 2 wherein the left atrium is paced at a specified  
5 offset interval preceding a left ventricular event.
8. The method of claim 6 wherein the specified AAL interval varies with heart rate.
- 10 9. The method of claim 7 wherein the specified offset interval varies with heart rate.
10. The method of claim 1 wherein the LA-LV interval is measured during implantation of a left ventricular lead.
- 15 11. A system for setting optimal pacing parameters for delivering cardiac resynchronization therapy in a biventricular pacing mode to a patient, comprising:  
an implantable cardiac rhythm management device for delivering  
20 biventricular pacing, wherein the device is programmed to deliver right and left ventricular paces separated by specified biventricular offset interval BVO and in an atrial tracking or AV sequential mode so that the ventricular paces are delivered at an atrio-ventricular delay interval AVD following an atrial event;  
means for measuring the time interval between a left atrial contraction  
25 and a left ventricular contraction in the patient, designated as the LA-LV interval;  
means for comparing the LA-LV interval to a specified threshold Th1 and identifying the patient as having a prolonged inter-atrial delay if the LA-LV interval is less than the threshold Th1; and,  
30 means for adjusting the manner in which the cardiac resynchronization therapy is delivered to compensate for the prolonged inter-atrial delay.

12. The system of claim 11 wherein the adjusting means includes means for initiating pacing of the left atrium if the LA-LV interval is less than the specified threshold Th1.
- 5 13 The system of claim 11 wherein the adjusting means includes means for delivering cardiac resynchronization therapy as biventricular pacing in an atrial tracking or AV sequential pacing mode with a specified atrio-ventricular (AVD) interval, with the AVD interval selected to be long enough to maintain adequate left atrial-left ventricular synchrony if the LA-LV interval is less than the  
10 threshold Th1.
14. The system of claim 13 further comprising:  
means for varying the AVD interval while measuring a variable related to cardiac output; and,  
15 means for setting the AVD interval to a value which maximizes the variable related to cardiac output.
15. The system of claim 14 wherein the AVD interval setting means is a controller of the implantable device programmed to automatically compute the  
20 optimum AVD value and set the AVD parameter to that value.
16. The system of claim 14 further comprising an external programmer for communicating with the implantable device via a wireless telemetry link and wherein the AVD interval setting means is the external programmer which is  
25 programmed to automatically compute the optimum AVD value and set the AVD parameter to that value in the implantable device.
17. The system of claim 12 wherein the left atrium is paced at a specified atrial-atrial delay (AAL) interval following a right atrial sense or pace.  
30
18. The system of claim 12 wherein the left atrium is paced at a specified offset interval preceding a left ventricular event.

19. The system of claim 17 wherein the specified AAL interval varies with heart rate.

20. The system of claim 18 wherein the specified offset interval varies with  
5 heart rate.

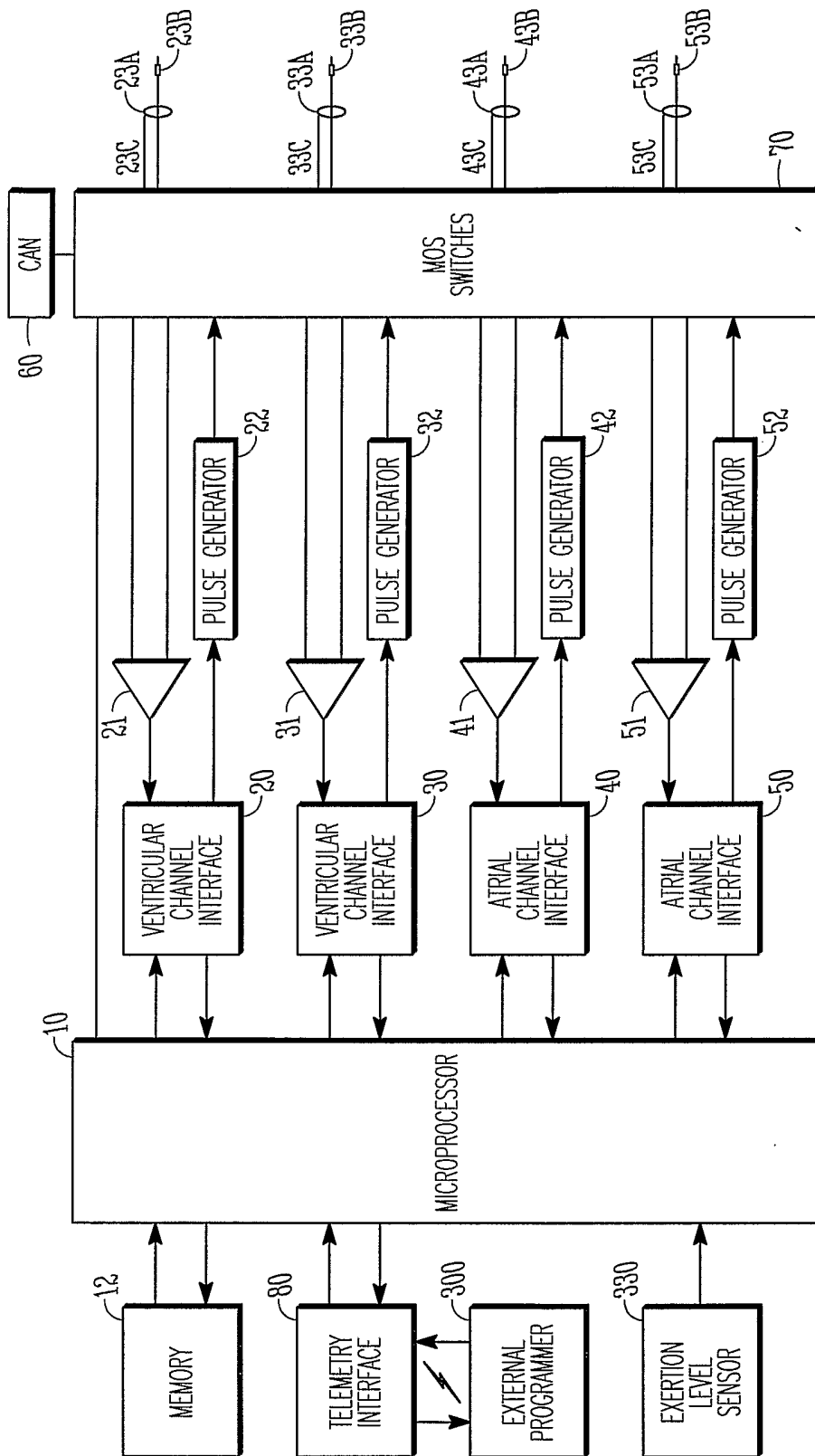


FIG. 1

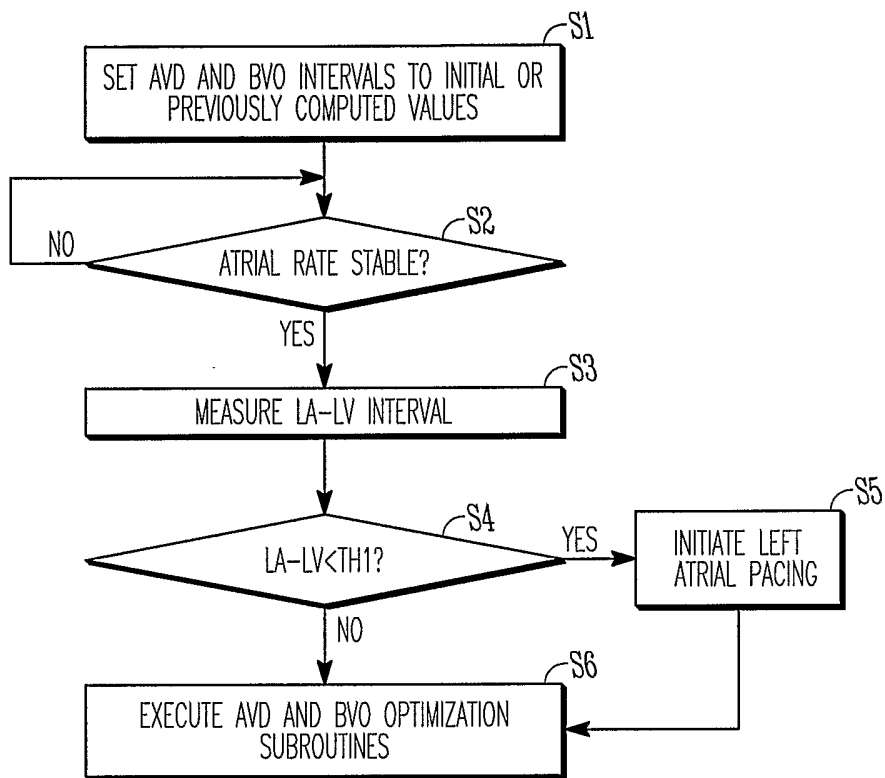


FIG. 2



## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/010287A. CLASSIFICATION OF SUBJECT MATTER  
INV. A61N1/362

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

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

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

EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                | Relevant to claim No. |
|-----------|---|-----------------------|
| X         | US 2003/083700 A1 (HILL MICHAEL R.S ET AL)<br>1 May 2003 (2003-05-01)                             | 11                    |
| Y         | paragraphs [0001], [0014] - [0016],<br>[0020], [0027], [0028]                                     | 12-20                 |
| Y         | US 2004/193223 A1 (KRAMER ANDREW P ET AL)<br>30 September 2004 (2004-09-30)<br>the whole document | 12-20                 |
| A         | US 5 902 324 A (THOMPSON ET AL)<br>11 May 1999 (1999-05-11)<br>abstract                           | 11-20                 |

 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 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

10 August 2006

Date of mailing of the international search report

21/08/2006

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2006/010287

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 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.  Claims Nos.: 1-10  
because they relate to subject matter not required to be searched by this Authority, namely:  
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 III Observations where unity of invention is lacking (Continuation of item 3 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.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/010287

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