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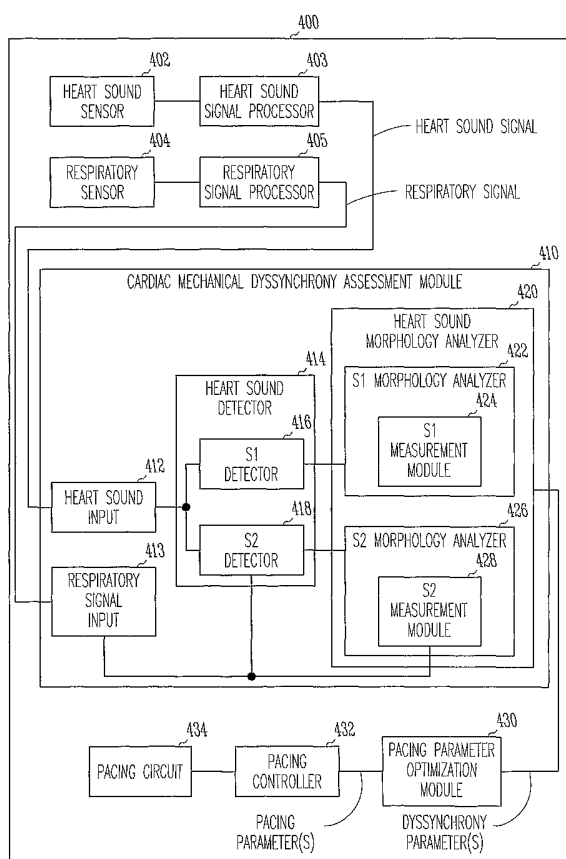SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
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(54) Title: METHOD AND APPARATUS FOR INDIVIDUAL INTRAVENTRICULAR DELAY OPTIMIZATION

(57) Abstract: A cardiac rhythm management system provides
for assessment of cardiac mechanical dyssynchrony based on
heart sound morphology and optimization of pacing parameters
based on the effect of pacing on the cardiac mechanical
dyssynchrony assessment. A degree of cardiac mechanical
dyssynchrony is measured by the time delay between tricuspid
valve closure and mitral valve closure and/or the time delay
between pulmonary valve closure and aortic valve closure. A
cardiac resynchronization therapy is optimized by determining
therapy parameters to provide an approximately minimum
degree of cardiac mechanical dyssynchrony by cardiac pacing.

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METHOD AND APPARATUS FOR INDIVIDUAL
INTRAVENTRICULAR DELAY OPTIMIZATION

Claim of Priority

5   Benefit of priority is hereby claimed to U.S. Patent Application Serial
Number 10/865,498, filed on June 10 2004, which application is herein
incorporated by reference.

Cross-Reference to Related Applications

10   This application is related to co-pending, commonly assigned, U.S.
Patent Application Serial No. 10/334,694, entitled "METHOD AND
APPARATUS FOR MONITORING OF DIASTOLIC HEMODYNAMICS,"
filed December 30, 2002, and U.S. Patent Application Serial No. 10/307,896,
"PHONOCARDIOGRAPHIC IMAGE-BASED ATRIOVENTRICULAR
15   DELAY OPTIMIZATION," filed December 2, 2002, which are hereby
incorporated by reference in their entirety.

Field of the Invention

This document generally relates to cardiac rhythm management (CRM)
20   systems and particularly, but not by way of limitation, to such systems providing
for optimization of cardiac therapy using heart sounds.

Background

The heart is the center of a person's circulatory system. It includes a
25   complex electro-mechanical system performing two major pumping functions.
The heart includes four chambers: right atrium (RA), right ventricle (RV), left
atrium (LA), and left ventricle (LV). The RA draws deoxygenated blood from
organs of the body and injects it into the RV through the tricuspid valve. The
RV pumps the deoxygenated blood to the lungs through the pulmonary valve.
30   The blood gets oxygenated in the lungs. The LA draws oxygenated blood from
the lungs and injects it into the LV through the mitral valve. The LV pumps the
oxygenated blood to the organs of the body, through the aortic valve, to provide
the organs with their metabolic needs for oxygen. These mechanical pumping
functions are accomplished by contractions of the myocardium (heart muscles).

In a normal heart, the sinoatrial (SA) node, the heart's natural pacemaker,
generates electrical impulses, called action potentials, that propagate through an
electrical conduction system to various regions of the heart to excite myocardial
tissues in these regions. Coordinated delays in the propagations of the action

5   potentials in a normal electrical conduction system cause the muscles in various
regions of the heart to contract in mechanical synchrony such that the pumping
functions are performed efficiently.

The normal pumping functions of the heart, indicated by the normal
hemodynamic performance, require a normal electrical system to generate the

10   action potentials and deliver them to designated portions of the myocardium with
proper timing, a normal myocardium capable of contracting with sufficient
strength, and a normal electro-mechanical association such that all regions of the
heart are excitable by the action potentials. A blocked or otherwise abnormal
electrical conduction and/or deteriorated myocardial tissue cause dysynchronous

15   contraction of the heart, resulting in poor hemodynamic performance, including
a diminished blood supply to the heart and the rest of the body. The condition
where the heart fails to pump enough blood to meet the body's metabolic needs
is known as heart failure.

Because the pumping functions are mechanical functions, the

20   hemodynamic performance is ultimately determined by the mechanical
synchrony of the heart. For this and other reasons, there is a need for a direct
assessment of cardiac mechanical dyssynchrony. The assessment serves as a
direct measure of efficacy for a cardiac therapy restoring the cardiac mechanical
synchrony.

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Summary

A cardiac rhythm management (CRM) system provides for assessment of
cardiac mechanical dyssynchrony based on heart sound morphology and
optimization of pacing parameters based on the effect of pacing on the cardiac

30   mechanical dyssynchrony assessment. A degree of cardiac mechanical
dyssynchrony is measured by the time delay between tricuspid valve closure and
mitral valve closure and/or the time delay between pulmonary valve closure and
aortic valve closure. A cardiac resynchronization therapy is optimized by

determining therapy parameters to provide an approximately minimum degree of cardiac mechanical dyssynchrony by cardiac pacing.

In one embodiment, a system for analyzing a heart includes a heart sound input, a heart sound detector, and a computer-based heart sound morphology

5   analyzer. The heart sound input receives one or more signals indicative of heart sounds. The heart sound detector detects heart sounds of at least one predetermined type. The computer-based heart sound morphology analyzer produces at least one dyssynchrony parameter indicative of a degree of cardiac mechanical dyssynchrony based on measurements of the detected heart sounds.

10   The heart sound morphology analyzer includes a heart sound measurement module to measure one or more parameters each based on at least one morphological feature of the detected heart sounds. The morphological feature indicates a time interval between closures of a first cardiac valve and a second cardiac valve of the heart in one cardiac cycle.

15   In one embodiment, a system for analyzing a heart includes an implantable system and an external system communicating with the implantable system. The implantable system includes one or more implantable heart sound sensors and an implantable medical device. The one or more implantable heart sound sensors sense one or more heart sound signals each indicative of heart

20   sounds. The implantable medical device includes an implant controller to process the one or more heart sound signals and an implant telemetry module to transmit the one or more heart sound signals to the external system. The external system includes an external telemetry module to receive the one or more heart sound signals and an external controller to process the one or more heart sound

25   signals. The external controller includes a heart sound morphology analyzer to produce at least one dyssynchrony parameter indicative of a degree of cardiac mechanical dyssynchrony. The heart sound morphology analyzer includes a heart sound measurement module to measure one or more parameters each based on at least one morphological feature of heart sounds of at least one

30   predetermined type. The morphological feature indicates a time interval between closures of a first cardiac valve and a second cardiac valve of a heart in one cardiac cycle.

In one embodiment, a method for operating a cardiac pacemaker is provided. One or more heart sound signals indicative of heart sounds are

received. Heart sounds of at least one predetermined type are detected. One or more dyssynchrony parameters each indicative of a degree of cardiac mechanical dyssynchrony are produced based on at least one morphological feature of the detected heart sounds by executing an automated cardiac mechanical

5   dyssynchrony algorithm. One or more pacing parameters for minimizing the degree of cardiac mechanical dyssynchrony are determined based on the one or more dyssynchrony parameters.

This Summary is an overview of some of the teachings of the present application and not intended to be an exclusive or exhaustive treatment of the

10   present subject matter. Further details about the present subject matter are found in the detailed description and appended claims. Other aspects of the invention will be apparent to persons skilled in the art upon reading and understanding the following detailed description and viewing the drawings that form a part thereof, each of which are not to be taken in a limiting sense. The scope of the present

15   invention is defined by the appended claims and their equivalents.

Brief Description of the Drawings

In the drawings, which are for illustrative purposes only and not necessarily drawn to scale, like numerals describe similar components

20   throughout the several views. The drawings illustrate generally, by way of example, but not by way of limitation, various embodiments discussed in the present document.

FIG. 1 is a graph illustrating a sensed heart sound signal before and after envelope detection.

25   FIG. 2 is a graph illustrating heart sound signals indicative of cardiac mechanical synchrony sensed by various heart sound sensors.

FIG. 3 is a graph illustrating heart sound signals indicative of cardiac mechanical dyssynchrony sensed by various heart sound sensors.

FIG. 4 is a block diagram illustrating one embodiment of a system for

30   optimizing pacing parameters based on a cardiac mechanical dyssynchrony assessment.

FIG. 5 is an illustration of one embodiment of a CRM system and portions of the environment in which the CRM system is used.

FIG. 6 is a block diagram illustrating one embodiment of a circuit of the CRM system.

FIG. 7 is a flow chart illustrating one embodiment of a method for optimizing pacing parameters based on the cardiac mechanical dyssynchrony assessment.

Detailed Description

In the following detailed description, reference is made to the accompanying drawings which form a part hereof, and in which is shown by way of illustration specific embodiments in which the invention may be practiced. These embodiments are described in sufficient detail to enable those skilled in the art to practice the invention, and it is to be understood that the embodiments may be combined, or that other embodiments may be utilized and that structural, logical and electrical changes may be made without departing from the spirit and scope of the present invention. The following detailed description provides examples, and the scope of the present invention is defined by the appended claims and their equivalents.

It should be noted that references to "an", "one", or "various" embodiments in this disclosure are not necessarily to the same embodiment, and such references contemplate more than one embodiment.

This document discusses, among other things, a method and system for optimizing therapies based on mechanical performance of the heart as indicated by heart sounds. Heart sounds, or generally energies resulted from the heart's mechanical vibrations, indicate the heart's mechanical activities, including the openings and closures of the tricuspid, pulmonary, mitral, and aortic valves. Because hemodynamic performance is ultimately determined by the mechanical synchrony of the heart, heart sounds provide a direct measure of efficacy for a therapy intended to restore the heart's ability to contract in synchrony.

Throughout this document, "heart sound" includes audible and inaudible mechanical vibrations caused by cardiac mechanical activities that can be sensed with an accelerometer. S1 generally refers to a heart sound type known as the "first heart sound," or as one or more occurrences or instances of the first heart sound, depending on the context. S2 generally refers to a heart sound type known as the "second heart sound," or as one or more occurrences or instances

of the second heart sound, depending on the context. A "user" includes a physician or other caregiver who examines and/or treats a patient using one or more of the methods and apparatuses reported in the present document.

FIG. 1 is a graph illustrating a sensed heart sound signal 100 and a processed heart sound signal 102 over one cardiac cycle. Both signals 100 and 102 indicate S1 and S2. Sensed heart sound signal 100 represents an output of a heart sound sensor such as an accelerometer sensing the heart's mechanical vibrations or a microphone sensing audible sound originated from the heart. The signal is conditioned by at least envelope detection to produce heart sound signal 102. In the system and method descriptions below, a "heart sound signal" refers to either a heart sound signal as an output of a heart sound sensor, such as illustrated by signal 100, or a heart sound signal that has been envelope detected, such as illustrated by signal 102.

Each cardiac cycle includes a diastolic phase, during which blood fills the RV through the tricuspid valve and the LV through mitral valve, and a systolic phase, during which the blood are ejected from the RV through the pulmonary valve and the LV through the aortic valve. S1 is known to originate from, among other things, the mechanical vibrations associated with tricuspid valve closure and mitral valve closure, which start the diastolic phase. S2 is known to originate from, among other things, the mechanical vibrations associated with pulmonary valve closure and aortic valve closure, which start the systolic phase.

FIG. 2 is a graph illustrating heart sound signals indicative of cardiac mechanical synchrony sensed by various heart sound sensors over a cardiac cycle. A "global" heart sound signal 202G is sensed by a single heart sound sensor sensing heart sounds originated from the entire heart. Heart sound signal 202G indicates $S1_G$ (global S1) and $S2_G$ (global S2) for heart that contracts synchronously. $S1_G$ is morphologically characterized by a single peak and an S1 width 210 that falls within the normal S1 width range. $S2_G$ is morphologically characterized by a single peak and an S2 width 212 that falls within the normal S2 width range.

"Regional" heart sound signals 202R and 202L are sensed simultaneously using two sensors each primarily sensing heart sounds originated from one portion of the heart, such as the right portion or the left portion. In one

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embodiment, heart sound signal 202R is sensed by a heart sound sensor placed within the RV, and heart sound signal 202L is sensed by a heart sound sensor placed within the LV. RV heart sound signal 202R indicates $S1_{RV}$ (S1 sensed in the RV) and $S2_{RV}$ (S2 sensed in the RV). $S1_{RV}$ indicates tricuspid valve closure.

5      $S2_{RV}$ indicates pulmonary valve closure. LV heart sound signal 202L indicates $S1_{LV}$ (S1 sensed in the LV) and $S2_{LV}$ (S2 sensed in the LV). $S1_{LV}$ indicates mitral valve closure. $S2_{LV}$ indicates aortic valve closure.

In a heart that contracts in synchrony, tricuspid valve closure ($S1_{RV}$) and mitral valve closure ($S1_{LV}$) occur substantially simultaneously. The sounds of

10   tricuspid valve closure and mitral valve closure substantially overlap, producing the normal $S1_G$. Pulmonary valve closure ($S2_{RV}$) and aortic valve closure ($S2_{RV}$) occur substantially simultaneously. The sounds of pulmonary valve closure and aortic valve closure substantially overlap, producing the normal $S2_G$.

FIG. 3 is a graph illustrating heart sound signals indicative of cardiac

15   mechanical dyssynchrony sensed by various heart sound sensors over a cardiac cycle. A "global" heard sound signal 302G is sensed by a single heart sound sensor sensing heart sounds originated from the entire heart. "Regional" heart sound signals 302R and 302L are sensed simultaneously using two sensors each primarily sensing heart sounds originated from one portion of the heart. Heart

20   sound signal 302G corresponds to heart sound signal 202G, heart sound signal 302R corresponds to heart sound signal 202R, and heart sound signal 302L corresponds to heart sound signal 202L. While signals 202G, 202R, and 202L illustrates heart sound signals indicative cardiac synchrony, signals 302G, 302R, and 302L illustrates heart sound signals indicative cardiac dyssynchrony.

25   When the cardiac muscles in various regions of the heart fail to contract in synchrony, i.e., when cardiac mechanical dyssynchrony occurs, relative timing between the valve closures deviates from their normal timing. A delay 314 between tricuspid valve closure ($S1_{RV}$) and mitral valve closure ($S1_{LV}$) indicates that the tricuspid valve and the mitral valve no longer close

30   substantially simultaneously. The delay results in a double peaked $S1_G$, and/or an abnormally large S1 width 310 associated with $S1_G$. A delay 316 between pulmonary valve closure ($S2_{RV}$) and aortic valve closure ($S2_{LV}$) indicates that the pulmonary valve and the aortic valve no longer close substantially simultaneously. The delay results in a double peaked $S2_G$, and/or an abnormally

large S2 width 312 associated with $S2_G$. Depends on individual conditions, a
heart that fails to contract in synchrony may be indicated by one or more of
delay 314 and delay 316 and/or one or more of S1 width 310 and S2 width 312.

It is to be understood that the relative timing between $S1_{RV}$ and $S1_{LV}$ and

5   the relative timing between $S2_{RV}$ and $S2_{LV}$ as shown in FIG. 3 represents an
example for illustrative purpose only. FIG. 3 shows exemplary heart sound
signals of a patient suffering left bundle branch block (LBBB), in which $S1_{RV}$
leads $S1_{LV}$ in time, and $S2_{RV}$ leads $S2_{LV}$ in time. However, the system and
method discussed below are generally applicable to cardiac mechanical

10   dyssynchrony indicated by any one or more of delay 314, delay 316, an
abnormally long S1 width 310, and an abnormally long S2 width 312.

An effective treatment to resynchronize the heart shortens or eliminates
either or both delays 314 and 316 and restores both widths 310 and 312 to their
normal values. In other words, the goals of the treatment include (i) merging the

15   two peaks of $S1_G$, and merging the two peaks of $S2_G$, or (ii) realigning $S1_{RV}$ and
$S1_{LV}$, and realigning $S2_{RV}$ and $S2_{LV}$. In case the goal with respect to S1 and the
goal with respect to S2 cannot be both met, higher priority is given to the goal of
(i) merging the two peaks of $S2_G$, or (ii) realigning $S2_{RV}$ and $S2_{LV}$.

One example of such treatment is the application of cardiac

20   resynchronization therapy (CRT), which resynchronizes the contractions of the
heart, particularly the ventricles, by delivering ventricular pacing pulses using
proper timing. The extent to which a therapy restores cardiac synchrony is
indicated by the extent to which delay 314 or 316 are reduced, or by the extent to
which width 310 and 312 returned to their normal values.

25   In system and method descriptions below, heart sound signals 302G,
302R, and 302L, and heart sounds $S1_G$, $S2_G$, $S1_{RV}$, $S2_{RV}$, $S1_{LV}$, and $S2_{RV}$ are
used for illustrative, but not restrictive, purposes. Heart sound signal 302G
generally includes a "global" heart sound sensed by a single sensor and
indicative of heart sounds originating from anywhere in the heart. Heart sound

30   signals 302R and 302L include two heart sound signals simultaneously by two
sensors. Heart sound signal 302R generally includes a "regional" heart sound
indicative of primarily heart sounds originating from the right side of the heart,
sensed by such as a sensor placed in the RV. Heart sound signal 302L generally
includes another "regional" heart sound indicative of primarily heart sounds

originating from the left side of the heart, sensed by such as a sensor placed in the LV. $S1_G$ generally includes a heart sound resulted from a combination of tricuspid valve closure and mitral valve closure. $S2_G$ generally includes a heart sound resulted from a combination of pulmonary valve closure and aortic valve

5   closure. $S1_{RV}$ generally includes a heart sound resulted from tricuspid valve closure. $S2_{RV}$ generally includes a heart sound resulted from pulmonary valve closure. $S1_{LV}$ generally includes a heart sound resulted from mitral valve closure. $S2_{LV}$ generally includes a heart sound resulted from aortic valve closure. S1 generally refers to the heart sound type known as the "first heart

10   sound," or as one or more occurrences of the "first heart sounds," including $S1_G$, $S1_{RV}$, and $S1_{LV}$. S2 generally refers to a heart sound type known as the "second heart sound," or as one or more occurrences of the "second heart sounds," including $S2_G$, $S2_{RV}$, and $S2_{RV}$.

        FIG. 4 is a block diagram illustrating one embodiment of a system 400

15   for optimizing pacing parameters based on a cardiac mechanical dyssynchrony assessment. System 400 includes a heart sound sensor 402, a heart sound signal processor 403, a respiratory sensor 404, a respiratory signal processor 405, a cardiac mechanical dyssynchrony assessment module 410, a pacing parameter optimization module 430, a pacing controller 432, and a pacing circuit 434. In

20   one embodiment, portions of system 400 are implemented as a computer-based system.

        Heart sound sensor 402 includes one or more sensors each sense a signal indicative of heart sounds. Examples of the one or more sensors include accelerometers and microphones. In one embodiment, heart sound sensor 402

25   includes a single heart sound sensor to sense a heart sound signal 302G. In one specific embodiment, the single heart sound sensor is placed external to the heart. In another specific embodiment, the single heart sound sensor is placed within a heart chamber. In another embodiment, heart sound sensor 402 is a sensor system including a plurality of heart sound sensors each sensing a signal

30   indicative of heart sounds originating from a particular portion of the heart. In one specific embodiment, the plurality of heart sound sensors include an RV heart sound sensor to sense heart sound signal 302R and an LV heart sound sensor to sense heart sound signal 302L. In one specific embodiment, the RV heart sound sensor is an intracardiac heart sound sensor for placement in the RV

to sense a heart sound signal indicative of at least tricuspid valve closure and
pulmonary valve closure, and the LV heart sound sensor is another intracardiac
heart sound sensor for placement in the LV to sense a heart sound signal
indicative of at least mitral valve closure and aortic valve closure. In another
5   specific embodiment, the RV heart sound sensor is the intracardiac heart sound
sensor for placement in the RV to sense the heart sound signal indicative of at
least tricuspid valve closure and pulmonary valve closure, and the LV heart
sound sensor is an epicardial heart sound sensor for placement on the epicardial
wall over the LV to sense a heart sound signal indicative of at least mitral valve
10   closure and aortic valve closure.

Heart sound signal processor 403 conditions the one or more heart sound
signals sensed by heart sound sensor 402. Heart sound signal processor 403
includes an envelope detector to produce heart sound signal 302G and/or heart
sound signals 302R and 302L. In one embodiment, heart sound signal processor
15   403 further includes an ensemble averaging circuit to improve a signal-to-noise
ratio of each of the one or more heart sound signals by ensemble averaging.

Respiratory sensor 404 senses a respiratory signal indicative of
respiratory cycles each including an inspiratory phase and expiratory phase. In
one embodiment, respiratory sensor 404 includes an accelerometer sensing an
20   acceleration signal indicative of inspiration and expiration. In another
embodiment, respiratory sensor 404 includes a minute ventilation sensor. In one
specific embodiment, the minute ventilation sensor is an implantable impedance
sensor sensing a thoracic impedance indicative of minute ventilation.

Respiration signal processor 405 conditions the respiratory signal for use
25   by cardiac mechanical dyssynchrony assessment module 410. In one
embodiment, respiration signal processor 405 includes an expiration detector to
detect and indicate each expiratory phase of the respiratory cycle.

Cardiac mechanical dyssynchrony assessment module 410 produces one
or more dyssynchrony parameters each indicative of a degree of cardiac
30   mechanical dyssynchrony based on at least the one or more heart sound signals
sensed by heart sound sensor 402 and preprocessed by heart sound signal
processor 403. Cardiac mechanical dyssynchrony assessment module 410
includes a heart sound input 412, a respiratory signal input 413, a heart sound
detector 414, and a heart sound morphology analyzer 420. In one embodiment,

cardiac mechanical dyssynchrony assessment module 410 is implemented as a computer-based system. In one specific embodiment, cardiac mechanical dyssynchrony assessment module 410 produces the one or more dyssynchrony parameters by executing an automated cardiac mechanical dyssynchrony

5   algorithm using at least the one or more heard sound signals and/or detected S1 and S2 as input.

Heart sound input 412 receives the one or more heart sound signals, such as heart sound signal 302G and/or heart sound signals 302R and 302L. Respiratory signal input 413 receive the respiratory signal indicative of which

10   occurrences of $S2_G$ and/or $S2_{RV}$ and $S2_{LV}$ are detected during an expiratory phase.

Heart sound detector 414 detects heart sounds from the one or more heart sound signals. Heart sound detector 414 includes at least an S1 detector 416 and an S2 detector 418. In one embodiment, S1 detector 416 detects $S1_G$, and S2

15   detector 418 detects $S2_G$, both from heart sound signal 302G. In another embodiment, S1 detector 416 detects $S1_{RV}$ from heart sound signal 302R and $S1_{LV}$ from heart sound signal 302L, and S2 detector 418 detects $S2_{RV}$ from heart sound signal 302R and $S2_{LV}$ from heart sound signal 302L.

Heart sound morphology analyzer 420 produces one or more

20   dyssynchrony parameters. In one embodiment, heart sound morphology analyzer 420 is a computer-based analyzer that produces the one or more dyssynchrony parameters by executing the automated cardiac mechanical dyssynchrony algorithm. The automated cardiac mechanical dyssynchrony algorithm is designed to detect morphological features of detected S1 and S2,

25   make measurements related to the morphological features, and produce the one or more dyssynchrony parameters based on results of the measurements, as described below.

Heart sound morphology analyzer 420 includes at least an S1 morphology analyzer 422 to produce a dyssynchrony parameter related to $S1_G$

30   (or $S1_{RV}$ and $S1_{LV}$) and an S2 morphology analyzer 426 to produce another dyssynchrony parameter related to $S2_G$ (or $S2_{RV}$ and $S2_{LV}$). In one embodiment, S2 morphology analyzer 426 to produce the dyssynchrony parameter related to $S2_G$ (or $S2_{RV}$ and $S2_{LV}$) based on only on $S2_G$ (or $S2_{RV}$ and $S2_{LV}$) detected during an expiratory phase of the respiratory cycle. Heart sound morphology

analyzer 420 includes one or more heart sound measurement modules to measure parameters associated with the morphological features of the one or more heart sounds. S1 morphology analyzer 422 includes an S1 measurement module 424. S2 morphology analyzer 426 includes an S2 width measurement module 428.

5   In one embodiment, each heart sound measurement module includes a heart sound width measurement module to measure widths of the heart sounds. S1 measurement module 424 includes an S1 width measurement module to measure S1 width 310 (the width of $S1_G$). S2 measurement module 428 includes an S2 width measurement module to measure S2 width 312 (the width of $S2_G$).

10   In another embodiment, each heart sound measurement module includes a heart sound delay measurement modules to measure delays in cardiac valve closure as indicated by heart sounds in a single heart sound signal such as heart sound signal 302G. Each heart sound delay measurement module includes a peak detector and a timer. The peak detector detects peaks within a heart sound

15   each indicating one valve closure. If two peaks are detected within the heart sound, the timer measures the delay as the time interval between the two peaks. In this embodiment, S1 measurement module 424 includes an S1 delay measurement measure to measure S1 delay 314 as a time interval between two peaks detected within $S1_G$. S2 measurement module 428 includes an S2 delay

20   measurement measure to measure S2 delay 316 as a time interval between two peaks detected within $S2_G$. In one embodiment, an imaging technique, such as tissue Doppler imaging (TDI), echocardiography, or magnetic resonance imaging (MRI), is applied to differentiate between the two peaks of $S1_G$. This provides for identification of the peak associated with tricuspid valve closure and

25   the peak associated with mitral valve closure in $S1_G$. Normally, the pulmonary valve closure is delayed during an inspiratory phase. In one embodiment, this fact is utilized to differentiate between the two peaks of $S2_G$. This provides for identification of the peak associated with pulmonary valve closure and the peak associated with aortic valve closure in $S2_G$. In one embodiment, each heart

30   sound measurement modules of morphology analyzer 420 is calibrated on a periodic basis or as needed using these peak identification techniques.

        In another embodiment, each heart sound measurement module includes a heart sound delay measurement modules to measure delays in cardiac valve closure as indicated by heart sounds in two heart sound signals such as heart

sound signals 302R and 302L. Each heart sound delay measurement module
includes a timer to measure the delay being a time interval between a heart
sound detected in one heart sound signal and the heart sound detected in another
heart sound signal. In this embodiment, S1 measurement module 424 includes

5   an S1 delay measurement module to measure S1 delay 314 as the time interval
between $S1_{RV}$ and $S1_{LV}$. S2 measurement module 428 includes an S2 delay
measurement module to measure S2 delay 316 as the time interval between $S2_{RV}$
and $S2_{LV}$.

In another embodiment, heart sound morphology analyzer 420 includes a

10   heart sound time-frequency analyzer to produce at least one time-frequency
representation for each of the one or more heart sound signals and produce the
one or more dyssynchrony parameters each associated with at least one feature
of the one time-frequency representation. In one embodiment, the heart sound
time-frequency analyzer further produces a parameter indicative of pulmonary

15   artery pressure based on at least one feature of the time-frequency
representation. The heart sound time-frequency analyzer includes, by way of
example, and not by way of limitation, one or more of a short-time Fourier
transform (STFT) module, a reduced interference (RID) module, and a wavelet
transform (WT) module. The STFT module produces a time versus frequency

20   representation of the signal by applying a sliding window to data representing
the one or more heart sound signals. A spectral representation based on a
windowed Fourier transform (FT) is computed each time the window position is
updated. The RID module provides an improvement in resolution over the
STFT based on the Wigner-Ville time-frequency distribution by presenting a

25   result with reduced interference. The WT module takes advantage of the fact
that higher frequencies are better resolved in time while lower frequencies are
better resolved in frequency. This processing involves recursively filtering the
data representing the one or more heart sound signals at different scales with sets
of high-pass and low-pass filters.

30   Pacing parameter optimization module 430 determines one or more
approximately optimal pacing parameters based on the one or more
dyssynchrony parameters. The approximately optimal pacing parameters
provide for an approximately minimum degree of cardiac mechanical
dyssynchrony. Pacing controller 432 controls the delivery of pacing pulses to

the heart from pacing circuit 434 using parameters provided by pacing parameter
optimization module 430 for evaluating the parameters by their effects on the
degree of cardiac mechanical dyssynchrony. The approximately optimal pacing
parameters are determined by selecting parameters associated with the lowest

5   degree of degree of cardiac mechanical dyssynchrony, as indicated by the one or
more dyssynchrony parameters, from all the parameters evaluated.

        In one embodiment, pacing parameter optimization module 430
optimizes one or more pacing parameters by adjusting the one or more pacing
parameters for an approximately optimal value of each of the one or more

10   dyssynchrony parameters. The approximately optimal value is a value
associated with the minimum degree of cardiac mechanical dyssynchrony
obtained by the adjusting the one or more pacing parameters. Pacing parameter
optimization module 430 includes a parameter adjustment circuit to adjust the
one or more pacing parameters. The parameter adjustment circuit includes, but

15   is not limited to, one or more of a pacing site selector, an atrioventricular delay
(AVD) adjustment circuit, and an interventricular delay (IVD) adjustment
circuit. The pacing site selector selects one or more pacing sites to which the
pacing pulses are delivered. The AVD adjustment circuit adjusts one or more
AVDs at which ventricular pacing pulses are delivered. The IVD adjustment

20   circuit adjusts one or more IVDs at which ventricular pacing pulses are
delivered. After each adjustment of any one or more of the pacing sites, AVDs,
and IVDs, pacing controller 432 controls the delivery of the pacing pulses from
pacing circuit 434 using the adjusted parameters. The optimization process
includes repeated parameter adjustments and deliveries of pacing pulses using

25   the adjusted parameters until an approximately minimum or otherwise
satisfactory degree of cardiac mechanical dyssynchrony is reached.

        In another embodiment, pacing parameter optimization module 430
optimizes one or more pacing parameters by testing various combinations of
values for the one or more pacing parameters for their effects on the degree of

30   cardiac mechanical dyssynchrony. Pacing parameter optimization module 430
includes a parameter generator to generate a plurality of pacing parameter value
sets each including a value for each of the one or more pacing parameters. The
parameter generator includes, but is not limited to, one or more of a pacing site
generator, an AVD generator, and an IVD generator. The pacing site generator

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generates a plurality of pacing sites or pacing site combinations to which the pacing pulses are delivered. The AVD generator generates a plurality of AVDs at which ventricular pacing pulses are delivered. The IVD generator generates a plurality of IVDs at which ventricular pacing pulses are delivered. In one

5   embodiment where more than one pacing parameter is being tested, each of the pacing parameter value sets includes a unique combination of values for the tested parameters. Pacing controller 432 controls the delivery of a plurality of pacing pulse sequences from pacing circuit 434. Each sequence includes a plurality of pacing pulses delivered using one of the pacing parameter value sets.

10   The optimization process includes identifying the pacing parameter value set that produces an approximately minimum or otherwise satisfactory degree of cardiac mechanical dyssynchrony. In one embodiment, pacing parameter optimization module 430 includes an optimal parameter selector to select an optimal parameter value set associated with the minimum degree of cardiac mechanical

15   dyssynchrony produced by pacing during the optimization process.

       It is to be understood that while optimization of pacing parameters, and particularly the pacing sites, AVDs, and IVDs are discussed as examples, the idea of adjusting or optimizing a therapy using a measure of cardiac mechanical dyssynchrony is not limited to the optimization of pacing therapy. The basic

20   concept of adjusting or optimizing a therapy by determining therapy parameters providing for a minimum degree of cardiac mechanical dyssynchrony generally applies to the optimization of other pacing parameters and other therapies including, but not being limited to, other electrical therapies, physical therapies, chemical therapies, and biological therapies.

25   FIG. 5 is an illustration of one embodiment of a cardiac rhythm management (CRM) system 500 and portions of the environment in which system 500 is used. System 500 includes an implantable system 505, an external system 555, and a telemetry link 540 providing for communication between implantable system 505 and external system 555.

30   Implantable system 505 includes, among other things, implantable medical device 510 and lead system 508. In various embodiments, implantable medical device 510 is an implantable CRM device including one or more of a pacemaker, a cardioverter/defibrillator, a cardiac resynchronization therapy (CRT) device, a cardiac remodeling control therapy (RCT) device, a drug

delivery device, and a biological therapy device. In one embodiment, implantable medical device 510 includes implantable sensors for sensing the signals used by cardiac mechanical dyssynchrony assessment module 410 and pacing parameter optimization module 430. In another embodiment, implantable

5 medical device 510 and lead system 508 each include one or more of the implantable sensors. As shown in FIG. 5, implantable medical device 510 is implanted in a body 502. Lead system 508 provides connections between implantable medical device 510 and a heart 501. In various embodiments, lead system 508 includes leads for sensing physiological signals and delivering

10 pacing pulses, cardioversion/defibrillation shocks, and/or pharmaceutical or other substances. In one embodiment, at least one implantable sensor is incorporated into a lead of lead system 508 for placement in or about heart 501.

In one embodiment, external system 555 is a patient management system including external device 550, network 560, and remote device 570. External

15 device 550 is within the vicinity of implantable medical device 510 and communicates with implantable medical device 510 bi-directionally via telemetry link 540. Remote device 570 is in a remote location and communicates with external device 550 bi-directionally via network 560, thus allowing a user to monitor and treat a patient from a distant location. In another

20 embodiment, external system includes a programmer communicating with implantable medical device 510 bi-directionally via telemetry link 540.

System 500 includes system 400 for optimizing pacing parameters based on the cardiac mechanical dyssynchrony assessment. In one embodiment, system 500 also serves diagnostic and/or other therapeutic purposes by providing

25 the user with heart sound signals indicative of cardiac mechanical dyssynchrony and/or other cardiovascular conditions. The distribution of system 400 in system 500 depends on design and patient management considerations, such as the size and power consumption of each system component and the ability of monitoring the patient in various settings from various locations. In one embodiment,

30 implantable medical device 510 includes the entire system 400. In another embodiment, implantable medical device 510 includes portions of system 400, and external system 555 includes the remaining portions of system 400. One specific embodiment is discussed below with reference to FIG. 6 as an example, but not a limitation.

FIG. 6 is a block diagram illustrating one embodiment of a circuit of system 500, including implantable system 505, external system 555, and telemetry link 540 wirelessly coupling the two systems.

Implantable system 505 includes lead system 508, heart sound sensor
5   402, respiratory sensor 404, and implantable medical device 510. Lead system 508 includes pacing leads each having at least one electrode to be placed in a heart chamber. Each pacing lead allows delivery of pacing pulses to, and sensing of cardiac electrical activity from, a cardiac location where the electrode is placed. In one embodiment, lead system 508 includes one or more atrial
10   pacing leads and one or more ventricular pacing leads. The one or more atrial pacing leads include at least one RA pacing lead. The one or more ventricular pacing leads include one or more RV pacing lead and/or one or more LV pacing leads. In one embodiment, heart sound sensor 402 includes one sensor housed in implantable medical device 510 to sense heart sound signal 302G. In another
15   embodiment, heart sound sensor 402 includes one intracardiac sensor incorporated into a pacing lead of lead system 508 for placement within a heart chamber to sense heart sound signal 302G. In another embodiment, heart sound sensor 402 includes one intracardiac sensor incorporated into an RV pacing lead to sense heart sound signal 302R and another intracardiac sensor or epicardial
20   sensor incorporated into an LV pacing lead to sense heart sound signal 302L. In one embodiment, respiratory sensor 404 is housed in implantable medical device 510. In another embodiment, respiratory sensor 404 is incorporated into a pacing lead of lead system 508 for placement within a heart chamber.

Implantable medical device 510 includes pacing circuit 434, a sensing circuit
25   603, an implant controller 636, and an implant telemetry module 642. Pacing circuit 434 produces pacing pulses and delivers the pacing pulses to the heart through lead system 508. Sensing circuit 603 senses electrograms indicative of cardiac electrical activities. Implant controller 636 includes at least pacing controller 432, heart sound signal processor 403, and respiratory signal processor
30   405. Pacing controller 432 controls pacing circuit 434 by executing a selected pacing algorithm using at least the cardiac activities sensed by sensing circuit 603 and pacing parameters programmed into implant controller 636 as inputs.

External system 555 includes an external telemetry module 644 and an external controller 652. External controller 652 includes cardiac mechanical

dyssynchrony assessment module 410 and pacing parameter optimization module 430. In one embodiment, in which external system 555 includes external device 550, network 560, and remote device 570, remote device 570 includes cardiac mechanical dyssynchrony assessment module 410 and pacing

5   parameter optimization module 430. This allows long-term therapy optimization performed by the user, or by system 500 automatically, in a location away from the patient's presence. In one embodiment, system 500 provides for therapy optimization on a continuous basis. In another embodiment, system 500 provides for therapy optimization on a predetermined schedule, such as on a

10   periodic basis. In another embodiment, system 500 provides for therapy optimization in response to a change of patient condition detected by or through implantable system 505. In another embodiment, system 500 provides for therapy optimization in response to a command entered by the user. The therapy optimization results in one or more optimal pacing parameter values to be

15   programmed into implant controller 636.

Implant telemetry module 642 and external telemetry module 644 support telemetry link 540. Telemetry link 540 is a wireless bidirectional data transmission link. In one embodiment, telemetry link 540 is an inductive couple formed when two coils—one connected to implant telemetry module 642 and the

20   other connected to external telemetry module 644—are placed near each other. In this embodiment, the patient or the user places the coil connected to external device 550 on body 502 over implantable medical device 510. In another embodiment, telemetry link 540 is a far-field radio-frequency telemetry link allowing implantable medical device 510 and external device 550 to

25   communicate over a telemetry range that is at least ten feet. In one embodiment, implant telemetry module 642 transmits the heart sound and respiratory signals acquired by implantable system 505, and external telemetry module 644 receives these signals.

FIG. 7 is a flow chart illustrating one embodiment of a method for

30   optimizing pacing parameters based on the cardiac mechanical dyssynchrony assessment. In one embodiment, the method is performed by system 400.

One or more heart sound signals indicative of at least S1 and S2 are sensed at 700. In one embodiment, the one or more heart sound signals include one or more acceleration signals indicative of the heart's mechanical vibrations.

In another embodiment, the one or more heart sound signals include one or more audio signals originated from the heart. In one embodiment, heart sound signal 302G is sensed at 700. In another embodiment, heart sound signals 302R and 302L are sensed at 700. In another embodiment, both heart sound signal 302G and heart sound signals 302R and 302L are sensed at 700. In one embodiment, a respiratory signal indicative of respiratory cycles each including an inspiratory phase and expiratory phase is also sensed. In one specific embodiment, the respiratory signal includes an impedance signal indicative minute ventilation.

The one or more heart sound signals are processed at 710. The process includes envelope-detecting the one or more heart sound signals by rectification and low-pass filtering. In one embodiment, each envelope-detected heart sound signal is ensemble averaged to improve its signal-to-noise ratio. In one embodiment, the respiratory signal is also processed at 710. The process includes detection of expiratory phases.

Cardiac mechanical dyssynchrony is assessed based on the one or more heart sound signals at 720. The one or more heart sound signals are received at 722. In one embodiment, the respiratory signal is also received at 722. In one embodiment, only $S2_G$, and/or $S2_{RV}$ and $S2_{LV}$, that occur during the expiratory phase of the respiratory cycle are used for the assessment of cardiac mechanical dyssynchrony. S1 and S2 are detected from the one or more heart sound signals at 724. In one embodiment, $S1_G$ and $S2_G$ are detected from heart sound signal 302G. In another embodiment, $S1_{RV}$ and $S2_{RV}$ are detected from heart sound signal 302R, and $S1_{LV}$ and $S2_{LV}$ are detected from heart sound signal 302L. One or more dyssynchrony parameters each indicative of the degree of cardiac mechanical dyssynchrony are produced based on morphological features of, or related to, S1 and S2 at 726. In one embodiment, an automated cardiac mechanical dyssynchrony algorithm is executed to detect morphological features of detected S1 and S2, make measurements related to the morphological features, and produce the one or more dyssynchrony parameters based on results of the measurements at 726. The morphological features indicate cardiac valve closure delays. In one embodiment, a first dyssynchrony parameter related to S1 and a second dyssynchrony parameter related to S2 are produced at 726. The production of the dyssynchrony parameters includes measuring one or more parameters associated with the morphological features.

In one embodiment, S1 width 310 and S2 width 312 are measured from
heart sound signal 302G. In another embodiment, S1 delay 314 and S2 delay
316 are measured from heart sound signal 302G. S1 delay 314 is measured as
the time interval between the peak of $S1_G$ associated with mitral valve closure

5   and the peak of $S1_G$ associated with tricuspid valve closure. S2 delay 316 is
measured as the time interval between the peak $S2_G$ associated with aortic valve
closure and the peak $S2_G$ associated with pulmonary valve closure. In another
embodiment, S1 delay 314 and S2 delay 316 are measured from heart sound
signals 302R and 302L. S1 delay 314 is measured as the time interval between

10     $S1_{RV}$ and $S1_{LV}$. S2 delay 316 is measured as the time interval between $S2_{RV}$ and
$S2_{LV}$. In another embodiment, at least one time-frequency representation for
each of the one or more heart sound signals is produced. The time-frequency
representation is produced by, for example, performing one or more of STFT,
RID, and WT. One or more dyssynchrony parameters are produced each based

15   on at least one feature in the time-frequency representation. In a further
embodiment, a parameter is produced to indicate pulmonary artery pressure
based on at least one feature in the time-frequency representation.

        One or more pacing parameters are optimized at 730, based on the one or
more dyssynchrony parameters produced at 726. The one or more parameters

20   are optimized when the one or more dyssynchrony parameters indicate an
approximately minimum degree of cardiac mechanical dyssynchrony. In one
embodiment, the one or more pacing parameters are optimized based on at least
one dyssynchrony parameter produced based on S2 measurements. The
optimization is to minimize the time interval between pulmonary valve closure

25   and aortic valve closure. In another embodiment, the one or more pacing
parameters are optimized based on at least one dyssynchrony parameter
produced based on S1 measurements. The optimization is to minimize the time
interval between tricuspid valve closure and mitral valve closure. In another
embodiment, the one or more pacing parameters are optimized based on

30   dyssynchrony parameters produced based on both S1 and S2 measurements. If
the time interval between pulmonary valve closure and aortic valve closure and
the time interval between tricuspid valve closure and mitral valve closure cannot
be minimized with the same one or more pacing parameters, the minimization of

the time interval between pulmonary valve closure and aortic valve closure has a higher priority.

In one embodiment, the one or more pacing parameters are adjusted for an approximately optimal value of each of the one or more dyssynchrony

5 parameters. The approximately optimal value is a value associated with an approximately minimum degree of cardiac mechanical dyssynchrony obtained by adjusting the one or more pacing parameters. Adjusting the one or more pacing parameters includes, but is not limited to, selecting one or more pacing sites to which the pacing pulses are delivered, adjusting one or more AVDs at

10 which ventricular pacing pulses are delivered, and adjusting one or more IVDs at which ventricular pacing pulses are delivered. After each parameter adjustment, a plurality of pacing pulses is delivered to the heart using the one or more adjusted pacing parameters. The optimization process includes repeated parameter adjustments and delivery of pacing pulses using the adjusted

15 parameters until an approximately minimum or otherwise satisfactory degree of cardiac mechanical dyssynchrony is reached.

In another embodiment, the one or more pacing parameters are optimized by testing the effects of various combinations of values of the one or more pacing parameters on the one or more dyssynchrony parameters. A plurality of

20 pacing parameter value sets is generated. Each pacing parameter value set includes a value for each of the one or more pacing parameters. Generating the plurality of pacing parameter value sets includes, but is not limited to, generating a plurality of pacing sites or pacing site combinations to which pacing pulses are delivered, generating a plurality of AVDs at which ventricular pacing pulses are

25 delivered, and generating a plurality of IVDs at which ventricular pacing pulses are delivered. After the plurality of pacing parameter value sets are delivered, a plurality of pacing pulse sequences are delivered. Each sequence includes a plurality of pacing pulses delivered using one pacing parameter value set of the plurality of pacing parameter value sets. An optimal parameter value set is

30 selected from the plurality of pacing parameter value sets. The optimal pacing parameter value set is associated with an approximately optimal value of at least one of the one or more dyssynchrony parameters. The approximately optimal value is associated with a minimum degree of cardiac mechanical dyssynchrony obtained by pacing with the plurality of pacing parameter sets.

It is to be understood that the above detailed description is intended to be illustrative, and not restrictive. For example, the method for assessing the cardiac mechanical dyssynchrony can be performed by a non-implantable system. The method for optimizing pacing parameters can apply to optimization

5   of parameters of therapies other than cardiac pacing. Other embodiments, including any possible permutation of the system components discussed in this document, will be apparent to those of skill in the art upon reading and understanding the above description. The scope of the invention should, therefore, be determined with reference to the appended claims, along with the

10   full scope of equivalents to which such claims are entitled.

What is claimed is:

1.   A system for analyzing a heart having a first cardiac valve and a second
cardiac valve, the system comprising:

5   a heart sound input to receive one or more signals each indicative of heart
sounds;

        a heart sound detector, coupled to the heart sound input, to detect heart
sounds of at least one predetermined type from the one or more signals; and

        a computer-based heart sound morphology analyzer, coupled to the heart

10   sound detector, to produce at least one dyssynchrony parameter indicative of a
degree of cardiac mechanical dyssynchrony, the heart sound morphology
analyzer including a heart sound measurement module to measure one or more
parameters each based on at least one morphological feature of the heart sounds
of the at least one predetermined type, the at least one morphological feature

15   indicative of a time interval between closures of the first cardiac valve and the
second cardiac valve in one cardiac cycle.

2.   The system according to claim 1, wherein the heart sounds of the at least
one predetermined type comprise the first heart sounds (S1), and wherein the

20   heart sound morphology analyzer comprises an S1 morphology analyzer to
produce a first dyssynchrony parameter related to S1, the S1 morphology
analyzer including an S1 measurement module to measure one or more
parameters each based on at least an S1 morphological feature indicative a first
time interval between a tricuspid valve closure and a mitral valve closure.

25

3.   The system according to claim 1, wherein the heart sounds of the at least
one predetermined type comprise the second heart sounds (S2), and wherein the
heart sound morphology analyzer comprises an S2 morphology analyzer to
produce a second dyssynchrony parameter related to S2, the S2 morphology

30   analyzer including an S2 measurement module to measure one or more
parameters each based on at least an S2 morphological feature indicative of a
second time interval between a pulmonary valve closure and an aortic valve
closure.

4.   The system according to claim 1, wherein the heart sound input receives one or more signals indicative of first heart sounds (S1) and second heart sounds (S2), the heart sound detector detects S1 and S2, and the heart sound morphology analyzer comprises:

5   an S1 morphology analyzer to produce a first dyssynchrony parameter related to S1, the S1 morphology analyzer including an S1 measurement module to measure one or more parameters each based on at least an S1 morphological feature indicative a first measured time interval between a tricuspid valve closure and a mitral valve closure; and

10   an S2 morphology analyzer to produce a second dyssynchrony parameter related to S2, the S2 morphology analyzer including an S2 measurement module to measure one or more parameters each based on at least an S2 morphological feature indicative of a second measured time interval between a pulmonary valve closure and an aortic valve closure.

15

5.   The system according to claim 4, wherein the heart sound input comprise:

a right-ventricular heart sound input to receive a signal indicative of at least S1 sensed from a right ventricle ($S1_{RV}$) and S2 sensed from the right

20   ventricle ($S2_{RV}$); and

a left-ventricular heart sound input to receive a signal indicative of at least S1 sensed from a left ventricle ($S1_{LV}$) and S2 sensed from the left ventricle ($S2_{LV}$), and wherein:

the S1 heart sound measurement module comprises an S1 delay

25   measurement module to measure an S1 delay being a time interval between $S1_{RV}$ and $S1_{LV}$; and

the S2 heart sound measurement module comprises an S2 delay measurement module to measure an S2 delay being a time interval between $S2_{RV}$ and $S2_{LV}$.

30

6.   The system according to claim 5, further comprising a first implantable heart sensor adapted to sense the signal indicative of at least $S1_{RV}$ and $S2_{RV}$ and a second implantable heart sensor adapted to sense the signal indicative of at least $S1_{LV}$ and $S2_{LV}$.

7.   The system according to any of claims 4 to 6, wherein:

the S1 heart sound measurement module comprises an S1 width measurement module to measure an S1 width; and

the S2 heart sound measurement module comprises an S2 width

5   measurement module to measure an S2 width.

8.   The system according to any of claims 4 to 6, wherein:

the S1 heart sound measurement module comprises an S1 delay measurement module to measure an S1 delay being a time interval between a

10   morphological feature indicative of the tricuspid valve closure and a morphological feature indicative of the mitral valve closure; and

the S2 heart sound measurement module comprises an S2 delay measurement module to measure an S2 delay being a time interval between a morphological feature indicative of the pulmonary valve closure and a

15   morphological feature indicative of the aortic valve closure.

9.   The system according to any of claims 4 to 8, further comprising at least one implantable heart sound sensor to sense a signal indicative of at least S1 and S2.

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10.   The system according to claim 9, further comprising an ensemble averaging circuit to ensemble average the signal indicative of at least S1 and S2.

11.   The system according to any of claims 3 to 10, further comprising a

25   respiratory signal input to receive a respiratory signal indicative of an inspiratory phase and an expiratory phase of a respiratory cycle, and wherein at least the S2 heart sound measurement module is adapted to measure the one or more parameters during the expiratory phase.

30   12.   The system according to claim 11, further comprising an implantable respiratory sensor to sense the respiratory signal.

13.   The system according to claim 12, wherein the implantable respiratory sensor comprises an implantable accelerometer to sense an acceleration signal indicative of inspiration and expiration.

5   14.   The system according to claim 12, wherein the implantable respiratory sensor comprises an implantable impedance sensor to sense an impedance signal indicative of minute ventilation.

15.   The system according to any of the preceding claims, wherein the heart

10   sound morphology analyzer comprises a heart sound time-frequency analyzer to produce at least one time-frequency representation for each of the one or more signals and produce the at least one dyssynchrony parameter based on the at least one time-frequency representation.

15   16.   The system according to claim 15, wherein the heart sound time-frequency analyzer is adapted to further produce a parameter indicative of pulmonary artery pressure based on at least one feature in the at least one time-frequency representation.

20   17.   The system according to claim 15, wherein the heart sound time-frequency analyzer comprises a short-time Fourier transform (STFT) module.

18.   The system according to claim 15, wherein the heart sound time-frequency analyzer comprises a reduced interference (RID) module.

25

19.   The system according to claim 15, wherein the heart sound time-frequency analyzer comprises a wavelet transform (WT) module.

20.   The system according to any of the preceding claims, further comprising

30   a pacing parameter optimization module adapted to optimize one or more pacing parameters based on the at least one dyssynchrony parameter.

21.   The system according to claim 20, wherein the parameter optimization module is adapted to optimize one or more pacing parameters by adjusting the

one or more pacing parameters for an approximately optimal value for the at least one dyssynchrony parameter, and wherein the pacing parameter optimization module comprises a parameter adjustment circuit to adjust the one or more pacing parameters.

22.   The system according to claim 21, wherein the parameter adjustment circuit comprises a pacing site selector to select one or more pacing sites to which pacing pulses are delivered.

23.   The system according to any of claims 21 and 22, wherein the parameter adjustment circuit comprises an atrioventricular delay (AVD) adjustment circuit to adjust one or more AVDs at which ventricular pacing pulses are delivered.

24.   The system according to any of claims 21 to 23, wherein the parameter adjustment circuit comprises an interventricular delay (IVD) adjustment circuit to adjust one or more IVDs at which ventricular pacing pulses are delivered.

25.   The system according to claim 20, further comprising:
        a pacing circuit to deliver pacing pulses; and
        a pacing controller, coupled to the pacing circuit and the pacing parameter optimization module,
        wherein the pacing parameter optimization module comprises a pacing parameter generator to generate a plurality of pacing parameter sets each including one or more adjustable pacing parameters, and wherein the pacing controller is adapted to control a delivery of a plurality of the pacing pulse sequences each including a plurality of pacing pulses delivered using one pacing parameter set of the plurality of pacing parameter sets.

26.   The system according to claim 25, wherein the pacing parameter optimization module comprises an efficacy analyzer to relate each pacing parameter set of the plurality of pacing parameter sets to a value of the at least one dyssynchrony parameter.

27.   The system according to claim 26, wherein the pacing parameter

optimization module further comprises an optimal parameter selector to select an

optimal parameter set of the plurality of parameter sets, the optimal parameter

set associated with a minimum value of the at least one dyssynchrony parameter.

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28.   The system according to any of claims 25 to 27, wherein the pacing

parameter generator comprises a pacing site generator to generate a plurality of

pacing sites to one or more of which the pacing pulses are delivered.

10   29.   The system according to any of claims 25 to 28, wherein the pacing

parameter generator comprises an atrioventricular delay (AVD) generator to

generate a plurality of AVDs at which ventricular pacing pulses are delivered.

30.   The system according to any of claims 25 to 29, wherein the pacing

15   parameter generator comprises an interventricular delay (IVD) generator to

generate a plurality of IVDs at which ventricular pacing pulses are delivered.

31.   The system according to claim 1, further comprising:

        an implantable system including:

20   one or more implantable heart sound sensors to sense the one or

        more signals each indicative of heart sounds; and

                an implantable medical device including:

                        an implant controller, coupled to the one or more

                        implantable heart sound sensors, to process the one or more

25   signals; and

                        an implant telemetry module, coupled to the implantable

                controller, to transmit the one or more signals;

        an external system communicatively coupled to the implantable medical

        device, the external system including:

30   an external telemetry module to receive the one or more signals;

        and

                        an external controller coupled to the external telemetry module,

                        wherein the external controller includes the heart sound input, the

                heart sound detector, and the heart sound morphology analyzer.

32.   The system according to claim 31, wherein the implantable medical device comprises a hermetically sealed housing, and wherein at least one of the one or more heart sound sensors are housed within the hermetically sealed housing.

5

33.   The system according to claim 31, wherein the implantable medical device comprises a pacing circuit, and the implantable system further comprises one or more pacing leads coupled to the pacing circuit, wherein at least one of the one or more heart sound sensors is incorporated into the one of the one or

10   more pacing leads.

34.   The system according to claim 33, wherein the one or more pacing leads comprise a right ventricular (RV) pacing lead including at least an RV electrode and a left ventricular (LV) pacing lead include at least an LV electrode, wherein

15   the one or more heart sound sensors comprise an RV heart sound sensor incorporated into the RV pacing lead near the RV electrode and an LV heart sound sensor incorporated into the LV pacing lead near the LV electrode.

35.   The system according to any of claims 31 to 34, wherein the one or more

20   heart sound sensors comprise at least one accelerometer.

36.   The system according to any of claims 31 to 34, wherein the one or more heart sound sensors comprise at least one microphone.

25   37.   The system according to any of claims 31 to 36, wherein the implantable system further comprises a respiratory sensor to sense a respiratory signal indicative of respiratory cycles each including an inspiratory phase and expiratory phase, wherein the heart sound measurement module is adapted to measure the one or more parameters during the expiratory phase.

30

38.   The system according to claim 37, wherein the respiratory sensor comprises a minute ventilation impedance sensor incorporated onto the implantable medical device.

39.   The system according to claim 37, wherein the respiratory sensor comprises an accelerometer incorporated onto the implantable medical device.

40.   The system according to any of claims 31 to 40, wherein the external system comprise a patient monitoring system including:

        an external device communicatively coupled to the implantable medical device via telemetry;

        a telecommunication network coupled to the external device; and

        a remote device, coupled to the telecommunication network, to allow communication with the implantable medical device from a remote location.

41.   The system according to claim 40, wherein the heart sound morphology analyzer is included in the remote device.

42.   The system according to any of claims 31 to 41, wherein the external controller further comprise a pacing parameter optimization module adapted to optimize one or more pacing parameters based on the at least the dyssynchrony parameter.

43.   The system according to any of claims 31 to 42, wherein the implantable medical device comprises a cardiac resynchronization therapy (CRT) device.

44.   A method for operating a cardiac pacemaker, comprising:

        receiving one or more heart sound signals indicative of heart sounds of at least one predetermined type;

        detecting the heart sounds of the at least one predetermined type;

        producing one or more dyssynchrony parameters each indicative of a degree of cardiac mechanical dyssynchrony based on at least one morphological feature of the detected heart sounds of the at least one predetermined type by executing an automated cardiac mechanical dyssynchrony algorithm; and

        determining one or more pacing parameters for minimizing the degree of cardiac mechanical dyssynchrony based on the one or more dyssynchrony parameters.

45.   The method according to claim 44, further comprising sensing the one or more heart sound signals using one or more implantable heart sound sensors.

46.   The method according to claim 45, wherein sensing the one or more heart sound signals comprises sensing one or more acceleration signals.

47.   The method according to claim 45, wherein sensing the one or more heart sound signals comprises sensing one or more audio signals using one or more microphones.

48.   The method according to any of claims 45 to 47, wherein sensing the one or more heart sound signals comprises sensing a heart sound signal from a right ventricle (RV) and sensing another heart sound signal from a left ventricle (LV).

49.   The method according to any of claims 45 to 48, further comprising:
         producing an envelope of each of the one or more heart sound signals by rectifying and low-pass filtering the each of the one or more heart sound signals; and
         ensemble averaging each of the one or more heart sound signals to improve a signal-to-noise ratio of the each of the one or more heart sound signals.

50.   The method according to any of claims 45 to 49, wherein sensing the one or more heart sound signals comprises sensing one or more heart sound signals each indicative of at least first heart sounds (S1) and second heart sounds (S2).

51.   The method according to claim 50, wherein producing the one or more dyssynchrony parameters comprises producing a first dyssynchrony parameter related to S1 and producing a second dyssynchrony parameter related to S2.

52.   The method according to claim 51, further comprising:
         receiving a respiratory signal indicative of respiratory cycles each including an inspiratory phase and expiratory phase; and
         detecting the expiratory phase,

wherein producing the second dyssynchrony parameter related to S2
comprises producing the second dyssynchrony parameter related to S2 based on
at least one morphological feature of S2 detected during the expiratory phase.

5   53.   The method according to claim 52, further comprising sensing the
respiratory signal by sensing an thoracic impedance signal indicative minute
ventilation.

54.   The method according to claim 52, further comprising sensing the
10   respiratory signal by sensing an acceleration signal indicative of inspiration and
expiration.

55.   The method according to any of claims 51 to 54, wherein producing the
first dyssynchrony parameter related to S1 comprises measuring an S1 width,
15   and producing the second dyssynchrony parameter related to S2 comprises
measuring an S2 width.

56.   The method according to any of claims 51 to 54, wherein producing the
first dyssynchrony parameter related to S1 comprises measuring an S1 delay
20   representing a time interval between a tricuspid valve closure and a mitral valve
closure during one cardiac cycle, and producing the second dyssynchrony
parameter related to S2 comprises measuring an S2 delay representing delay
between a pulmonary valve closure and an aortic valve closure during one
cardiac cycle.

25

57.   The method according to any of claims 51 to 56, wherein producing the
first dyssynchrony parameter related to S1 comprises producing a time-
frequency representation of S1 and producing a first dyssynchrony parameter
associated with at least one feature in the time-frequency representation of S1,
30   and producing the first dyssynchrony parameter related to S2 comprises
producing a time-frequency representation of S2 and producing a second
dyssynchrony parameter associated with at least one feature in the time-
frequency representation of S2.

58.   The method according to claim 57, further comprising producing a parameter indicative of pulmonary artery pressure based on at least the time-frequency representation of S2.

5   59.   The method according to claim 57, wherein producing the time-frequency representation of S1 and the time-frequency representation of S2 each comprise performing a short-time Fourier transform (STFT).

60.   The method according to claim 57, wherein producing the time-
10   frequency representation of S1 and the time-frequency representation of S2 each comprise performing a reduced interference (RID).

61.   The method according to claim 57, wherein producing the time-frequency representation of S1 and the time-frequency representation of S2 each
15   comprise performing a wavelet transform (WT).

62.   The method according to any of claims 51 to 61, wherein determining the one or more pacing parameters comprises optimizing the one or more pacing parameters based on at least the second dyssynchrony parameter.
20
63.   The method according to claim 62, wherein determining the one or more pacing parameters further comprises optimizing the one or more pacing parameters based on the first dyssynchrony parameter.

25   64.   The method according to any of claims 44 to 63, further comprising delivering pacing pulses using the one or more pacing parameters.

65.   The method according to any of claims 44 to 64, wherein determining the one or more pacing parameters comprises adjusting the one or more pacing
30   parameters for an approximately optimal value of each of the one or more dyssynchrony parameters, the approximately optimal value being a value associated with an approximately minimum degree of cardiac mechanical dyssynchrony obtained by the adjusting the one or more pacing parameters.

66.   The method according to claim 65, wherein adjusting the one or more pacing parameters comprises selecting one or more pacing sites to which the pacing pulses are delivered.

5   67.   The method according to any of claims 65 and 66, wherein adjusting the one or more pacing parameters comprises adjusting one or more atrioventricular delays (AVDs) at which ventricular pacing pulses are delivered.

68.   The method according to any of claims 65 to 67, wherein adjusting the
10   one or more pacing parameters comprises adjusting one or more interventricular delays (IVDs) at which ventricular pacing pulses are delivered.

69.   The method according to any of claims 44 to 63, wherein determining the one or more pacing parameters comprises:

15   generating a plurality of pacing parameter sets each including one or more adjustable pacing parameters;

          delivering a plurality of the pacing pulse sequences each including a plurality of pacing pulses delivered using one pacing parameter set of the plurality of pacing parameter sets;

20   associating each pacing parameter set of the plurality of pacing parameter sets to a value of at least one of the one or more dyssynchrony parameters; and

          selecting an optimal parameter set of the plurality of parameter sets, the optimal parameter set associated with an optimal value of at least one of the one or more dyssynchrony parameters, the optimal value associated with a minimum

25   degree of cardiac mechanical dyssynchrony.

70.   The method according to claim 69, wherein generating the plurality of pacing parameter sets comprises generating a plurality of pacing sites to one or more of which the pacing pulses are delivered.

30

71.   The method according to any of claims 69 and 70, wherein generating the plurality of pacing parameter sets comprises generating a plurality of atrioventricular delays (AVDs) at which ventricular pacing pulses are delivered.
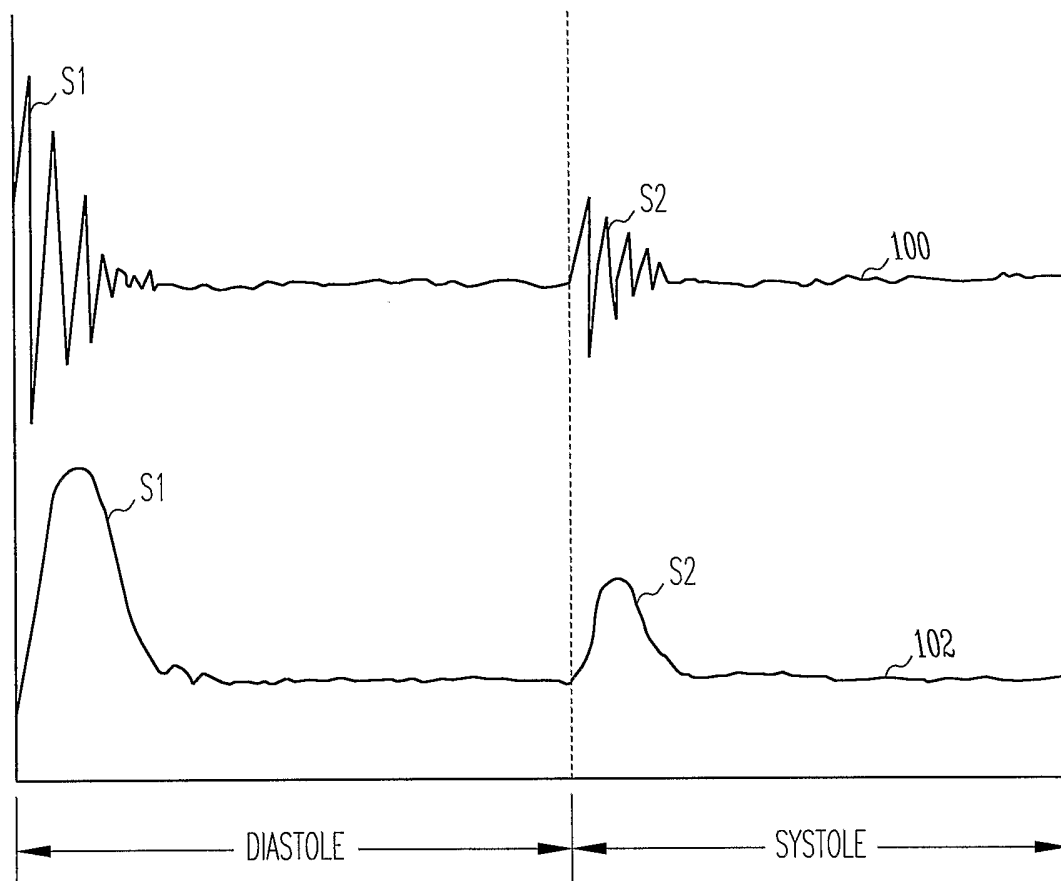
72.   The method according to any of claims 69 to 71, wherein generating the plurality of pacing parameter sets comprises generating a plurality of interventricular delays (IVDs) at which ventricular pacing pulses are delivered.
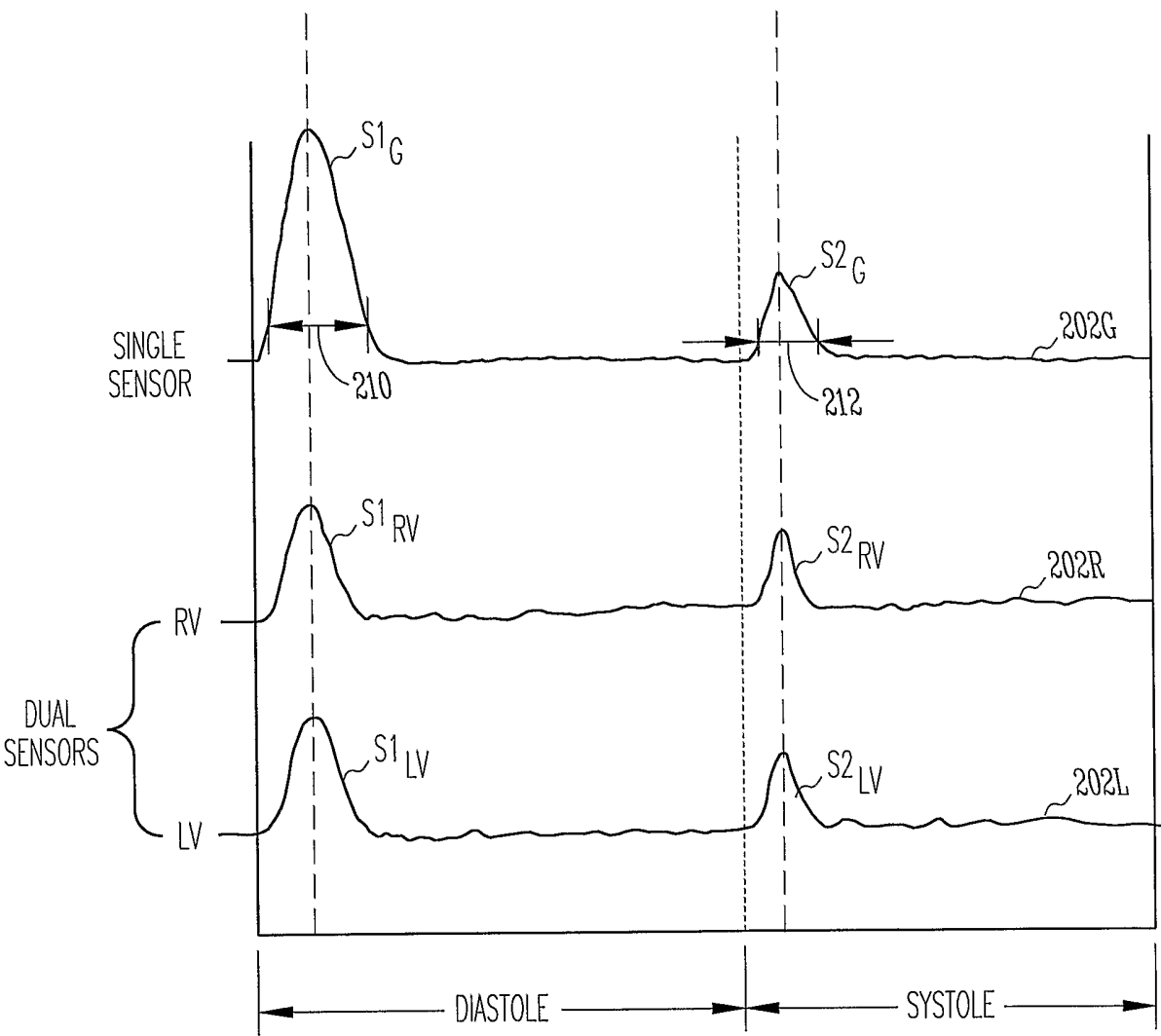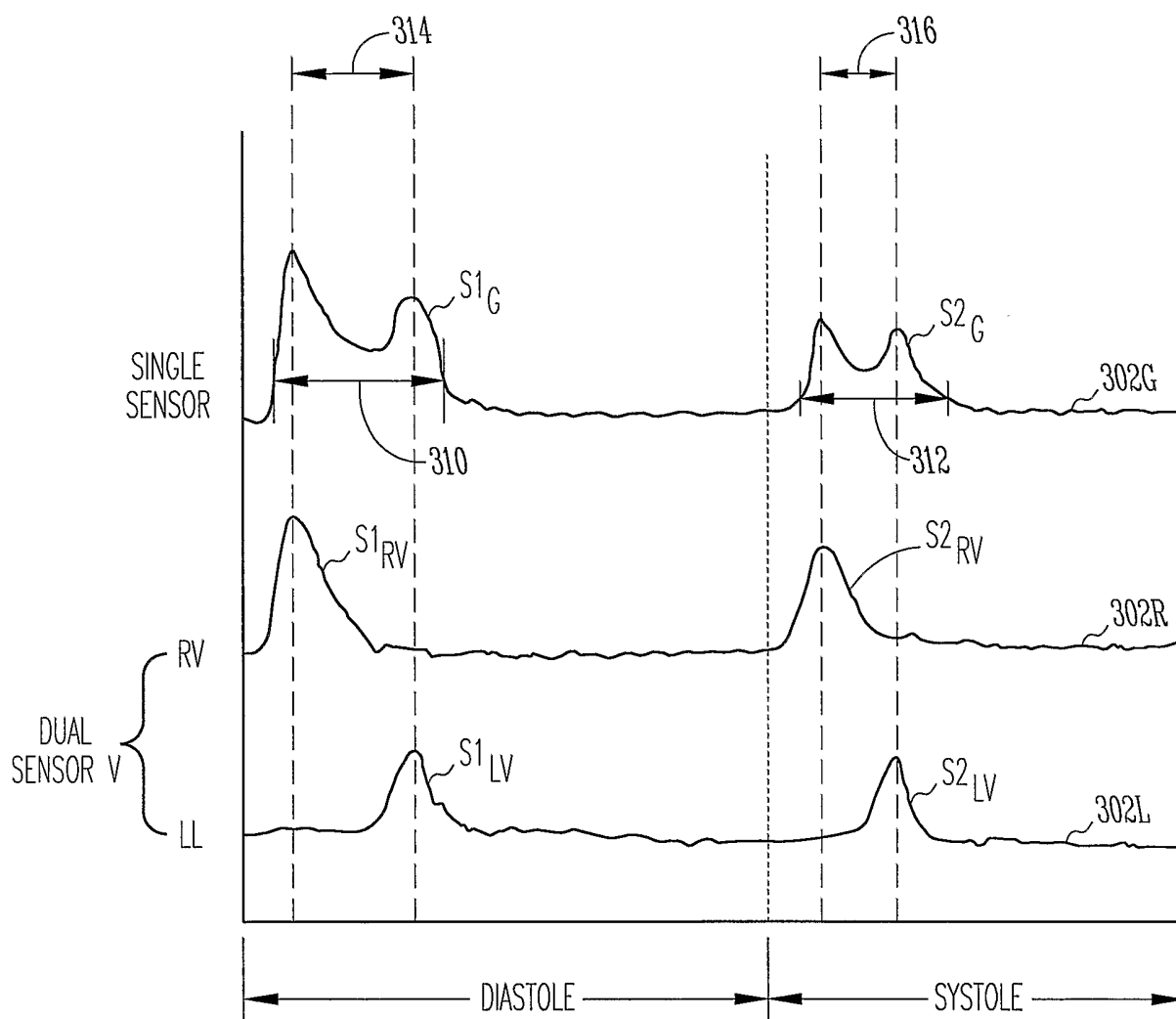
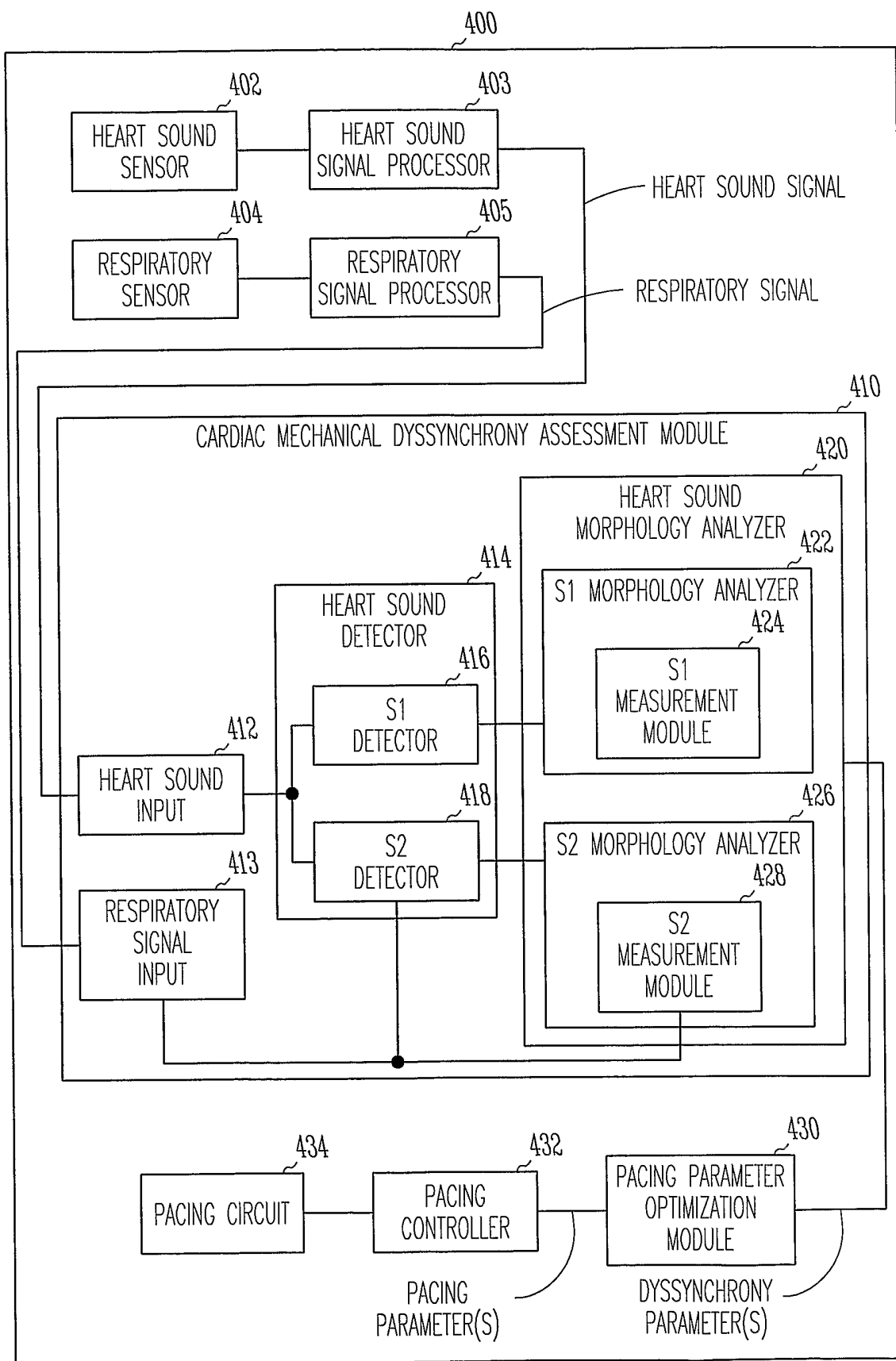Fig.1

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Fig.2

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Fig.3

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Fig.4
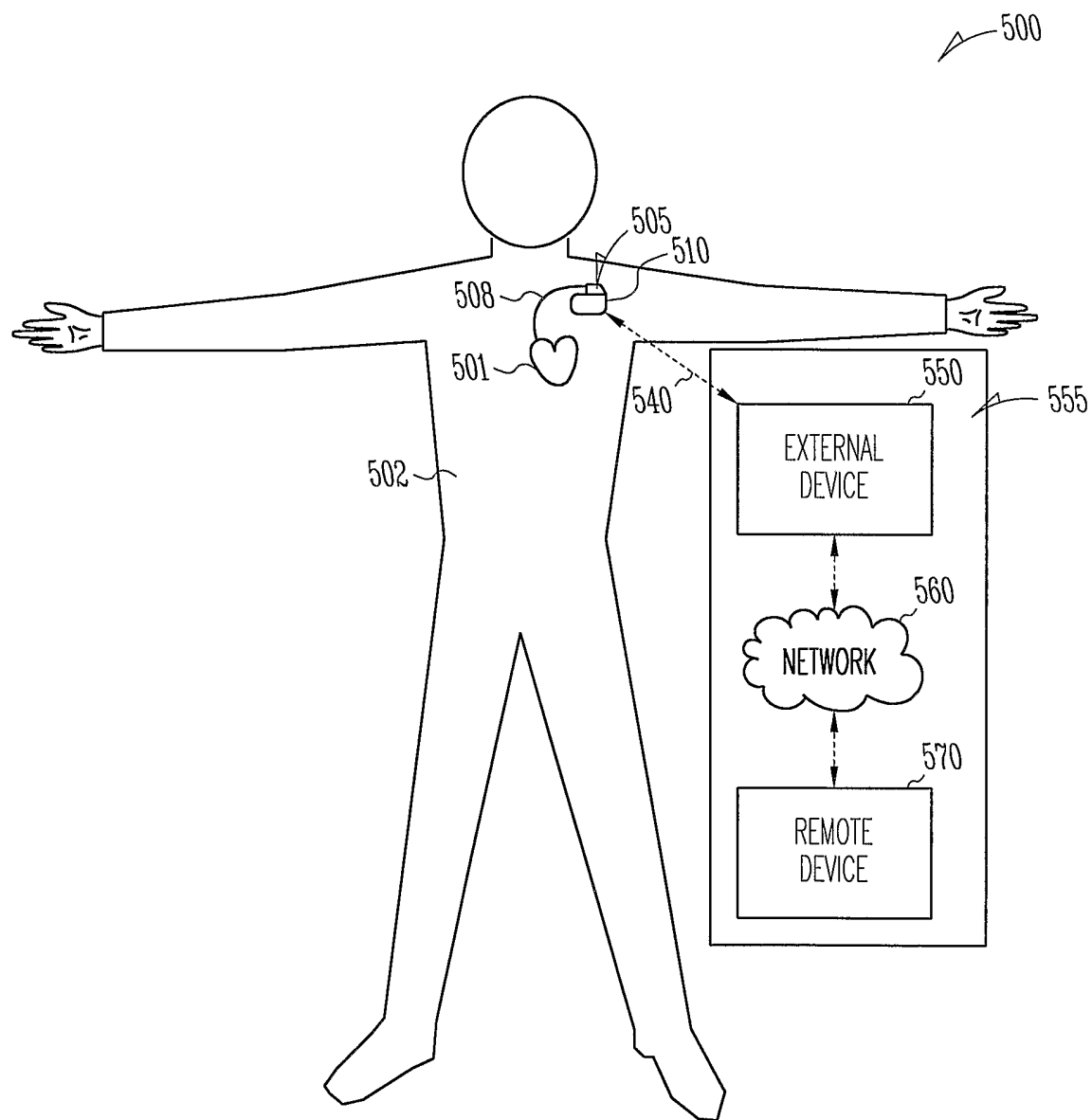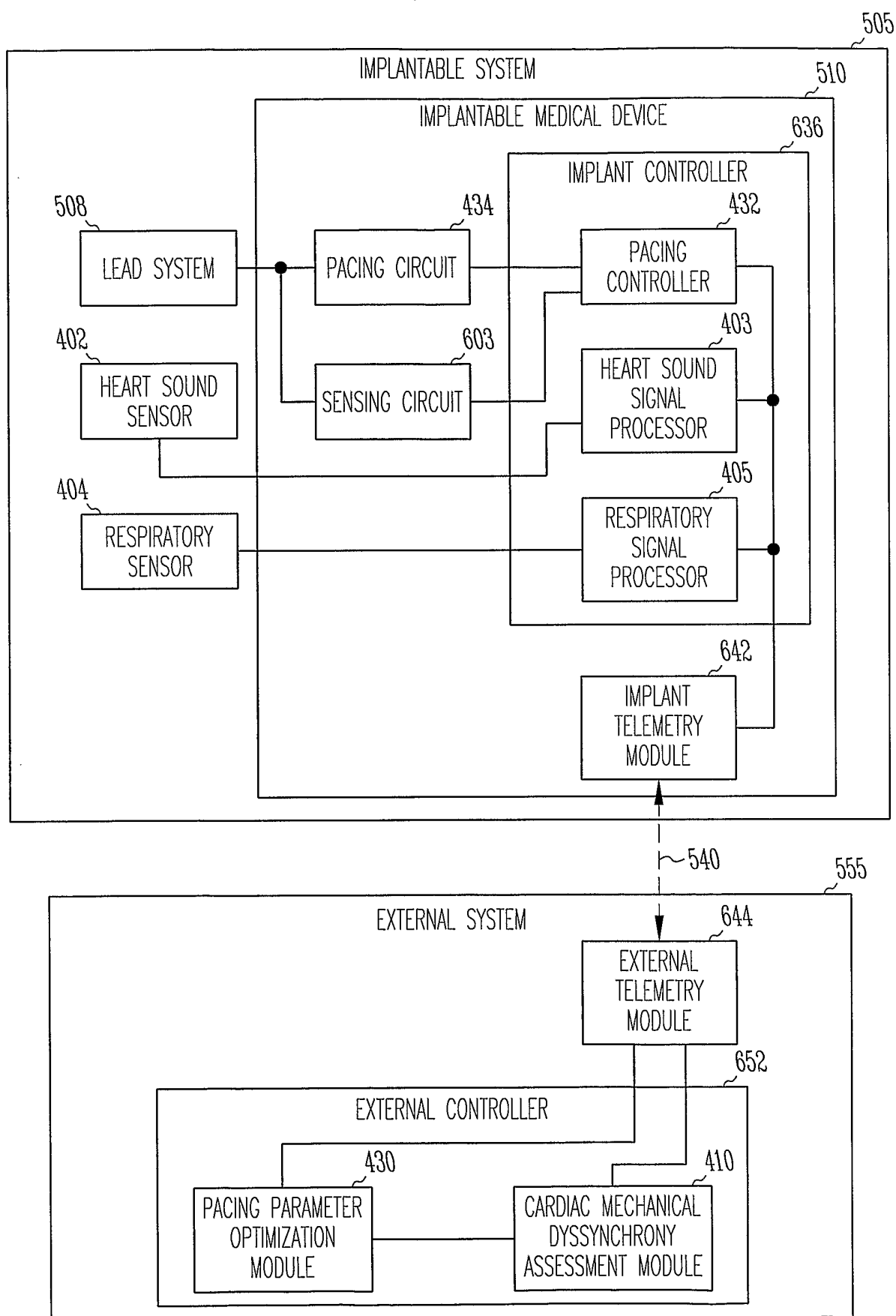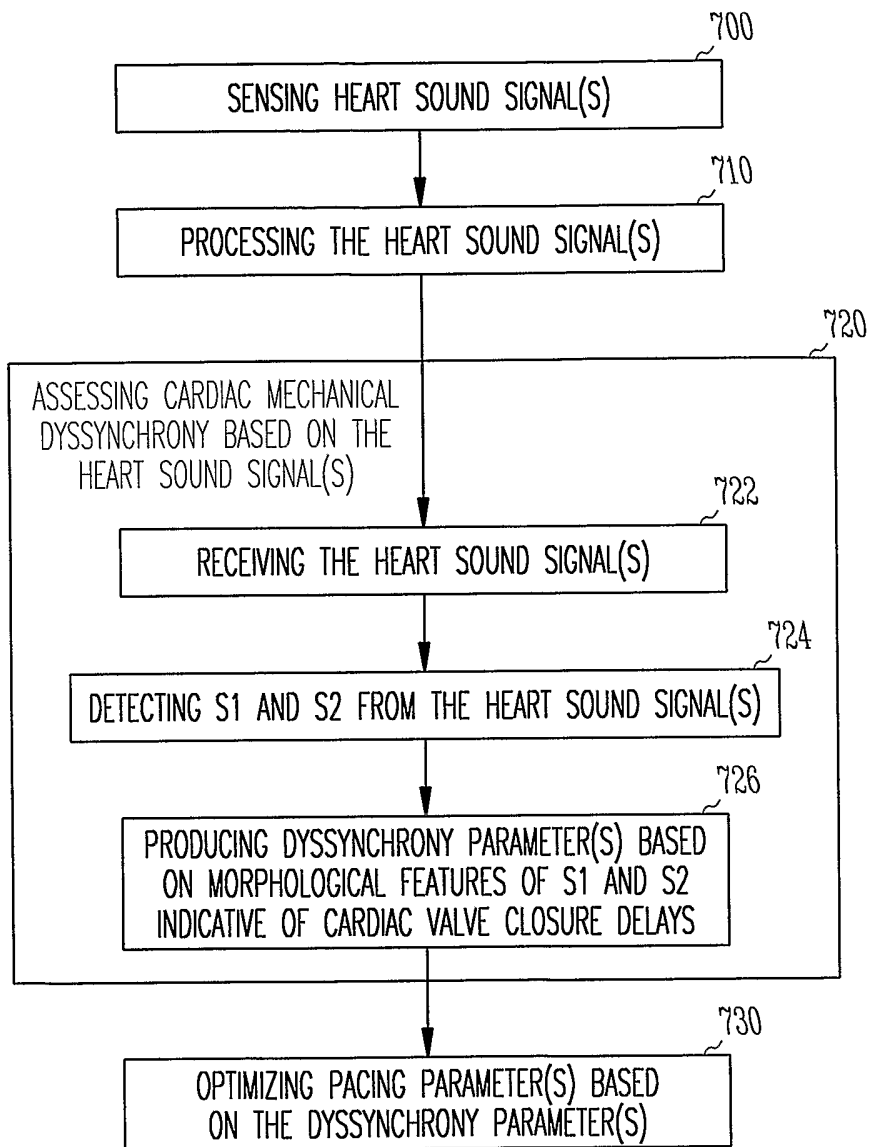
Fig.5

Fig.6

Fig.7

INT**E**RNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
A61B7/04   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)
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, 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 5 010 889 A (BREDESEN ET AL) 30 April 1991 (1991-04-30) column 2, line 64 - column 3, line 32; figures 1,2 column 6, lines 22,23 column 12, line 62 - column 13, line 18 column 15, lines 1-12 column 17, line 41 - column 18, line 44	1-5,7,8
A	column 35, lines 18-51	11
X	US 5 012 815 A (BENNETT, JR. ET AL) 7 May 1991 (1991-05-07) column 2, line 65 - column 3, line 31 column 4, lines 3-31; figures 3-5,8-11	1-5,7,8, 10,15-19
Y		6,9-14, 20-43

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☒ Further documents are listed in the continuation of box C.   ☒ Patent family members are listed in annex.

Date of the actual completion of the international search	Date of mailing of the international search report
18 October 2005	24/11/2005

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	Dhervé, G

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 6 643 548 B1 (MAI JUNYU ET AL) 4 November 2003 (2003-11-04) column 2, lines 13-43; figure 1 column 5, line 58 - column 6, line 32 column 6, line 66 - column 7, line 15 column 7, line 51 - column 8, line 41	6,9-14, 20-43
A	US 2004/106961 A1 (SIEJKO KRZYSZTOF Z ET AL) 3 June 2004 (2004-06-03) paragraphs '0007! - '0009!; figure 1 paragraphs '0030! - '0032!	6,20-36, 40-43
A	LEATHAM A.: "Splitting of the first and second heart sounds." LANCET, vol. 267, no. 6839, 25 September 1954 (1954-09-25), pages 607-614, XP008052982 ISSN: 0140-6736 the whole document	1-8, 11-14, 37-39
X	WOOD J C ET AL: "TIME-FREQUENCY TRANSFORMS: A NEW APPROACH TO FIRST HEART SOUND FREQUENCY DYNAMICS" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, IEEE SERVICE CENTER, PISCATAWAY, NJ, US, vol. 39, no. 7, 1 July 1992 (1992-07-01), pages 730-740, XP000294410 ISSN: 0018-9294 the whole document	1-10, 15-19, 31,35
X	BULGRIN J R; RUBAL B J; THOMPSON C R; MOODY J M: "Comparison of short-time Fourier, wavelet and time-domain analyses of intracardiac sounds." BIOMEDICAL SCIENCES INSTRUMENTATION, vol. 29, 1993, pages 465-472, XP008052978 USA the whole document	1-10, 15-19, 31,35
X	OBAIDAT M S ET AL: "Performance of the short-time Fourier transform and wavelet transform to phonocardiogram signal analysis" APPLIED COMPUTING: TECHNOLOGICAL CHALLENGES OF THE 1990'S. PROCEEDINGS OF THE 1992 ACM/SIGAPP SYMPOSIUM ON APPLIED COMPUTING ACM NEW YORK, NY, USA, 1992, pages 856-862, XP002349785 ISBN: 0-89791-502-X the whole document	1-10,15, 17,19

| 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. [X] Claims Nos.: 44-72
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 therapyRule 39.1(iv) PCT - Method for treatment of the human or animal body by surgeryRule 39.1(iv) PCT - Diagnostic method practised on the human or animal body

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

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