ACCELEROMETER-BASED MONITORING OF THE FREQUENCY DYNAMICS OF THE ISOVOLUMIC CONTRACTION PHASE AND PATHOLOGIC CARDIAC VIBRATIONS

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ABSTRACT

Methods and systems are disclosed that characterize cardiac function using an acceleration sensor to acquire and analyze the frequency dynamics associated with the isovolumic contraction phase ("ICP"). This information can be used to characterize heart function; optimize therapy for cardiomyopathy, including CRT therapy (including pacing intervals and required pharmacologic therapy); and to optimize CCM therapy. In addition, this information can be used to identify target pacing regions for CRT lead placement. Further, analyzing the frequency dynamics can be used to characterize pathologic heart vibrational motion, such as mitral regurgitation and the third or fourth heart sound, and the response of this motion to therapy for cardiomyopathy.
ABBREVIATIONS:

LV PRESS, LEFT VENTRICULAR PRESSURE
a, a-WAVE; c, c-WAVE; v, v-WAVE
ECG, ELECTROCARDIOGRAM
LVEDV, LEFT VENTRICULAR END-DIASTOLIC VOLUME
LVESV, LEFT VENTRICULAR END-SYSTOLIC VOLUME

I = FIRST HEART SOUND
II = SECOND HEART SOUND
III = THIRD HEART SOUND

Z = ISOVOLUMIC CONTRACTION PHASE

FIG. 1
PEAK FREQUENCY VS. dP/dt

CREATED USING DATA FROM IEEE TRANSACTION IN
BIOMEDICAL ENGINEERING, 39(7):730, JULY 1992

\[ y = 15.113x + 504.44 \]

\[ R^2 = 0.8498 \]

CORRELATION OF PEAK FREQUENCY DURING ISOVOLUMIC
CONTRACTION PHASE AND THE CHANGE IN PRESSURE
RISE IN THE LEFT VENTRICLE (dP/dt)

FIG. 2
FIG. 5
FIG. 7(A)

ELECTRODE FOR SURFACE ECG

FIG. 7(B)

SUB-PECTORALLY PLACED IAP

FIG. 7(C)

TRANSCEIVER CHIP

SIGNAL PROCESS AND CONTROL

MEMORY

3-AXIS ACCELEROMETER

SURFACE ELECTRODE
FIG. 8

LV ACCELERATION TO IDENTIFY OPTIMAL LEAD PLACEMENT

IMPROVING SYNCHRONY

ACCELERATION SIGNAL FREQUENCY (Hz)

ACCELERATION AMPLITUDE (mGs)

THRESHOLD

GOOD RESPONSE

POOR RESPONSE

ACCELERATION SIGNAL FREQUENCY (Hz)

ACCELERATION AMPLITUDE (mGs)

LV SITE #1

ACCEL SIGNAL

LV SITE #2

ACCEL SIGNAL

LV SITE #3

ACCEL SIGNAL

PEAK AMPLITUDE

PEAK FREQUENCY
ACCELEROMETER-BASED MONITORING OF THE FREQUENCY DYNAMICS OF THE ISOVOLUMIC CONTRACTION PHASE AND PATHOLOGIC CARDIAC VIBRATIONS

STATEMENT OF RELATED APPLICATIONS


[0002] This application is also related to U.S. patent application Ser. No. 11/318,325, filed Dec. 23, 2005, entitled “Devices and Methods For Accelerometer-Based Characterization of Cardiac Function and Identification of LV Target Pacing Zones,” which is incorporated by reference herein in its entirety.

BACKGROUND OF THE INVENTION

[0003] In prior provisional applications of the inventor, the use of acceleration sensors to monitor LV function (including the degree of mitral regurgitation) and to optimize cardiac resynchronization therapy (CRT) or cardiac contractility modulation therapy (CCM) was disclosed. In these applications, acceleration sensors, both wireless and conductively coupled, are integrated into disposable and implantable devices to monitor therapy for cardiomyopathy. In addition, sensors are integrated into a system for identifying target left ventricular (LV) pacing regions for CRT. The accelerometers are used to measure both vibration and displacement motion of the LV veins. The desired motion signal is acquired at the appropriate frequency, thus, displacement is measured at frequencies less than about 20 Hz, isovolumic contraction/relaxation vibrational motion is measured at frequencies of 20 Hz to 150 Hz, and vibrational motion related to mitral regurgitation is measured at frequencies greater than about 150 Hz. Various indices of LV function may be monitored including amplitudes and slopes of displacement motion, time intervals of vibrational motion, and changes in the time interval and frequency of mitral regurgitation signal.

[0004] Acceleration sensors have been previously disclosed for measuring the amplitude of acceleration signals during isovolumic contraction. Using a uniaxial accelerometer integrated into a right ventricular (RV) pacing lead, work done by Picchi et al. (“An implantable intracardiac accelerometer for monitoring myocardial contractility,” PACE 1996, 19:2066-2071) and others indicates that measurement of the peak amplitude of acceleration signals during the ICP correlates ventricular contractility and the rate of rise of ventricular pressure. Prior patent applications also disclose the measurement of peak amplitude acceleration signals to characterize contractility. For example, Chinchoy [US 2004/0172079 A1 and US 2004/0172078 A1] discloses the measurement of peak amplitude of the acceleration signal during the ICP from the LV epicardium to optimize the atriointerventricular (“AV”) delay and interventricular (“VV”) timing interval of a CRT device and to monitor long-term LV function. Yu et al. disclose the measurement of the phase shift in the peak amplitude of acceleration signals derived from the LV and RV to optimize AV and VV interval timing of a CRT device.

[0005] Accurate measurement of the peak amplitude of an acceleration signal using an acceleration sensor as discussed in prior disclosures, may be problematic due to variables that can affect the signal. One variable is the influence of the acceleration signal related to the gravitational field of the earth. This acceleration signal will change with the angle of tilt of the sensor relative to the gravitational acceleration vector. Thus, depending on the orientation of the sensor in the heart, the acceleration signal due to the earth’s gravity may increase or decrease the peak amplitude. Another factor which may affect the peak amplitude is the relative motion of the lead or catheter type device to which the acceleration sensor is affixed. Relative motion of the acceleration sensor device (e.g., a catheter LV lead) in the direction of acceleration may increase the signal amplitude and, if counter to the direction of myocardial acceleration, may reduce the peak amplitude. Further, if the axis of the acceleration sensor is not parallel to the axis of motion, the amplitude of the signal will also be reduced. Lastly, the motion of the heart due to respiration may affect the accuracy of the peak amplitude.

[0006] Further in the disclosures of Chinchoy and Yu [US 2003/0104596 A1], it is not clear if the sensor is measuring vibrational or displacement motion of the heart. Measurement of these different motion types requires signal acquisition in the appropriate frequency band; however, these prior disclosures do not indicate the acquired acceleration signal’s frequency band. Chinchoy indicates that the isovolumic contraction phase analyzed from the acceleration signal correlates with the S1 peak of myocardial Tissue Doppler velocity curve. However, this curve is a measurement of the displacement motion of the LV and therefore does not contain the vibrational component that may be more indicative of LV function. These above disclosures do not provide for measurement of pathologic vibrational motion, such as mitral regurgitation or the third/fourth heart sounds, and monitoring changes that may be indicative of improved LV function. Lastly, the above disclosures do not disclose a system and method for identifying target LV pacing sites for CRT through appropriate analysis of the ICP.

SUMMARY OF THE INVENTION

[0007] Monitoring changes in the frequency of the vibrational component of the ICP may be more practical and accurate than measuring amplitude changes for assessing cardiac function. Similarly, monitoring the time interval of this phase may prove more practical and accurate. Such an approach would reduce the sensitivity of the acceleration signal measurement and the interpretation of this measurement to the effects of gravity, sensor axis orientation, relative motion of the sensing device to which the sensor is affixed, and translational motion of the heart.

[0008] In this disclosure, systems characterize cardiac function using an acceleration sensor to acquire and analyze
the frequency dynamics associated with the isovolumic contraction phase ("ICP"). This information can be used to characterize heart function; optimize therapy for cardiomyopathy, including CRT therapy (including pacing intervals and required pharmacologic therapy); and to optimize CCM therapy. In addition, this information can be used to identify target pacing regions for CRT lead placement. Lastly, but not exhaustively, analyzing the frequency dynamics can be used to characterize pathologic heart vibrational motion, such as mitral regurgitation and the third or fourth heart sound, and the response of this motion to therapy for cardiomyopathy.

[0009] The system uses an acceleration sensor to characterize the frequency dynamics of the isovolumic contraction phase as it relates to contractility and ventricular function. In addition, the system measures pathologic heart vibrations such as mitral regurgitation and the third/fourth heart sounds and the effect of therapy on these signals. The sensor is placed into the ventricular chambers, onto the ventricular epicardium (e.g. LV), into the ventricular veins (e.g. the coronary sinus, great cardiac veins, or tributaries of this vein), or into the esophagus along the posterior side of the heart. The sensor can be integrated into an LV lead for CRT or CCM therapy for monitoring LV function. The sensor may also be incorporated into a catheter system for identifying target CRT pacing regions. The sensor may also be wireless and integrate into an implantable device (e.g. a stent) for long term monitoring of cardiac function.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] FIG. 1 shows a graph depicting various parameters of the cardiac pumping and ECG cycle.

[0011] FIG. 2 shows a graph depicting the correlation of peak frequency during the isovolumic contraction phase and the change in pressure rise in the left ventricle (dP/dt).

[0012] FIG. 3 shows vibrational acceleration signals from the epicardial surface of the left ventricle during isovolumic contraction, as measured with an accelerometer.

[0013] FIG. 4(A)-(E) shows a roving pacing guide wire device and acceleration-sensing catheter system for target pacing region identification and for characterizing the changes in LV function due to pacing.

[0014] FIG. 5 shows improved myocardial performance post-stimulation as determined by an increase in the peak frequency of the isovolumic contraction phase and a shortening of the time interval of the isovolumic contraction phase.

[0015] FIG. 6 shows shows myocardial motion mapping, display output, and target pacing identification.

[0016] FIG. 7 shows a subepicardial or subcutaneous implantable acceleration sensor with a wireless communications capability for monitoring S1, S2, S3, and S4 and murmur-related heart sounds.

[0017] FIG. 8 shows a graph indicating how the proper placement of an LV lead can be predicted using methods and devices according to embodiments of the invention.

DETAILED DESCRIPTION

[0018] A graph of the cardiac filling and pumping cycle and valvular events is shown in FIG. 1. The cardiac LV pumping cycle (LV cycle) is divided into two periods: diastole and systole. Diastole is the filling period and systole is the ejection period. Five different phases of the LV cycle can be identified within the systolic and diastolic periods: isovolumic contraction 56, ejection 58, isovolumic relaxation 62, early diastolic filling (rapid filling) 64, and late diastolic filling (atrial contraction) 66. Mitral valve closure 68 ("MVC") occurs during isovolumic contraction and aortic valve closure 72 ("AVC") occurs during isovolumic relaxation. Also shown in the figures are the left ventricular pressure LV Press 74, a regular electrocardiogram ECG 76, the left ventricular end-diastolic volume LVEDV 78, the left ventricular end-systolic volume LVESV 82, a graph depicting heart sounds 84, the left atrial pressure LA Press 86, the aortic pressure 88, a-wave 92, c-wave 94, and v-wave 96.

[0019] During the isovolumic contraction phase, the ventricles begin to contract but there is no ejection of blood into the aorta. As the myocardial cells contract, they generate a force that results in the development of wall tension in the ventricles. This contraction causes vibrational motion that is related to cardiac and ventricular resonance. This vibrational motion in its audible form is thought to be the cause the first heart sound and is associated with mitral valve closure. The vibrations may be related to abrupt changes in acceleration and direction of flow of the blood in the ventricular chamber.

[0020] In the normal heart, the isovolumic contraction starts within about 10-20 ms of ventricular depolarization (i.e., the R wave on the ECG), and lasts from about 30 milliseconds to 75 milliseconds depending on the heart rate and contractility of the ventricles. In the cardiomyopathic heart, the time interval of the isovolumic contraction phase is prolonged.

[0021] The frequency of the vibration motion that occurs during isovolumic contraction changes with the development of myocardial tension. Time-frequency transform analyses of this motion indicates that in the normal heart the frequency rises from about 20 Hz to about 150 Hz in the first 20-50 ms of the isovolumic contraction period. There are approximately 5-8 cycles that occur in this time period. Referring to FIG. 3, vibrational acceleration signals from the epicardial surface of the LV are shown during isovolumic contraction as measured with an accelerometer. The amplitudes of these cycles ranges from about 50 to 100 milliGs (1 G=9.8 m/sec^2) up to about 1 to 3 Gs.

[0022] Analysis of the frequency dynamics of the ICP can be used to characterize cardiac function. Thus the starting frequency of the ICP vibration motion signal, the peak frequency, and the time interval of change in frequency, may be affected by the mechanical and contractile properties of the ventricles. Peak frequency of this vibrational motion during ICP is probably related to the tension that develops in the ventricles and hence may be related to the contractility of the myocardium. Referring to FIG. 2, which shows the correlation of peak frequency during the isovolumic contraction phase and the change in pressure rise in the LV in dP/dt, a correlation between dP/dt (a surrogate for myocardial contractility) and the peak frequency during the ICP exists. The time interval over which this frequency rises may also be a measure of contractile function. The starting frequency during this phase may be related to the baseline ventricular wall tension.

[0023] In diseased hearts, such as those with cardiomyopathy, the contractile function of the myocardium is
reduced, and changes in the thickness and diameter of the LV can cause an increase in the wall tension. These changes also lead to an increase in the time interval of the isovolumic contraction phase. Therefore, monitoring changes in the frequency dynamics of the isovolumic contraction phase can give insights into the cardiac and LV function in cardiomyopathy patients. This frequency information may also be used to monitor the effects of therapy, such as CRT, and to identify target pacing regions in CRT. Similarly, monitoring changes in the time interval of the ICP can be indicative of cardiac function and the response to therapy. Because the frequency and time interval can be measured without having an accurate measure of amplitude, this approach may be preferred.

[0024] Similarly, vibrations from pathologic heart conditions may also be indicative of cardiac function and response to therapy. The frequency of the mitral regurgitation signal in cardiomyopathy is related to the degree of LV dilatation and the back flow of blood through the mitral valve. Therapies that reduce dilatation and or back flow, e.g., CRT or percutaneous anuloplasty, show a favorable response in the frequency and frequency dynamics of this vibration motion. The third or fourth heart sounds are also a vibrational motion that may be present in cardiomyopathy. Changes in the presence and frequency of these signal may be indicative of cardiac function and response to cardiomyopathy therapy. For example, the frequency dynamics of the S4 correlates with ventricular mass which can be indicative of worsening (increased mass) or improving (reduced mass) heart failure. The frequency of the S1 may also correlate with LV stiffness.

[0025] Accelerometer sensors are well suited for measuring ICP vibration motion and pathologic cardiac vibrational motion. The sensor is preferably based on micro electromechanical (MEMS) principles, which allows for miniaturization and low power consumption. The design and fabrication of capacitance MEMS-based accelerometers are known to those of ordinary skill in the art and may be used in this system. MEMS-based accelerometers are typically fabricated from silicon or semiconductor substrates. The sensor may be fabricated from a radiation-resistant semiconductor as the sensor will be implanted in many cases under fluoroscopic guidance. The general design of the accelerometer measures capacitance changes due to the movement of a proof mass beam with a side arm interdigitated between two capacitor plates. As the proof mass beam and side arm move with acceleration or vibration, the capacitance changes and can be output as a measure of motion. These accelerometers are fabricated from silicon substrates which allows for single-chip fabrication of the sensor with the necessary signal processing circuitry. This single-chip design increases the device's sensitivity as extremely small changes in capacitance can be measured. MEMS-based acceleration sensors as described above can measure milli Gs (1 G equals 9.8 meters/sec²) which is suitable for myocardial acceleration measurements which may occur between 50 and 2000 milli Gs or higher. While a capacitive sensor may be used in this embodiment, other acceleration sensor designs could be utilized and are known to those skilled in the art. For example, a thermal acceleration sensor could also be utilized in which the proof mass is a gas. Also, while a multi axis (2 or 3 axes) is preferred, single axis sensors could also be used and oriented appropriately to detect different axes of motion. It should also be noted that a pressure sensor can sense vibrational motion and may also be used to indirectly monitor the frequency dynamics of the ICP.

[0026] Preferably 3-axis sensing is utilized. A more accurate measurement of peak amplitude can be measured by calculating the composite acceleration vector of each axis (x, y, and z). This can account for the gravitational acceleration and its effects on sensor tilting. The composite vector can be calculated by taking the square root of the x-axis measurement squared, plus the y-axis measurement squared, plus the z-axis measurement squared. This peak amplitude calculation can be applied to both the vibrational motion and the displacement motion. This may be particularly accurate during the implantation of an LV lead for CRT therapy when the patient is lying still on a procedure table. Here the sensor measures the peak in the LV veins or coronary sinuses.

[0027] Vibrational motion related to ICP may be sensed in a frequency range greater than 20 Hz and up to 200 Hz. The sensors may be tuned to sense the desired range. Alternatively, band pass filters or digital signal processing could eliminate or reduce frequency bands that are lower or higher.

[0028] Sensors can be mounted on devices that access the heart or are disposed near the heart (e.g., via an esophageal probe) to optimally detect the desired ICP. In one embodiment, a uniaxial sensor is oriented such that the axis of acceleration is parallel to the radial plane of the heart, i.e., toward the center of the ventricular chamber. Alternatively, two uniaxial sensors could be oriented longitudinally, e.g., anatomically base to apex, and radially, or three uniaxial sensors, oriented longitudinally, radially, and laterally, may be used. A single triaxial sensor could measure all these components. In another embodiment, two dual-axis sensors are oriented perpendicularly to each other in the catheter or LV lead device. This provides three axes in the appropriate planes.

[0029] The acceleration sensor is coupled to a signal processing and powering module. A battery may be used to power the sensor but other sources may also be utilized. Acquisition of the signal may be triggered by a ventricular depolarization signal from a cardiac electrogram. For example, the R-wave from a surface cardiac electrogram (ECG) may serve as a trigger. The vibrational acceleration signal may then be acquired for about 100 ms. A shorter time interval for sampling could also be used (e.g., 50 ms) to focus in on the initial frequency associated with a rise in ventricular wall tension. A longer sampling interval may be used to acquire the mitral valve regurgitation and third/fourth heart sound signals. The R-wave or another signal of ventricular depolarization can also be used to provide a zero point for the acquisition of acceleration signals, and will also factor in the effects of gravity and tilt of the sensor. Thus, the accelerations signal measured around the time of the R-wave signal can be used as an off-set correction for subsequently acquired signals.

[0030] The signal may be first amplified by an isolation amplifier that provides an isolation barrier to reduce the potential for electric shock hazard. The signal may then be band-pass-filtered to remove low frequency (e.g. <20 Hz) and high frequency (e.g. >300 Hz) signals. The signal may then be subject to processing, both digital and analog, to characterize and identify the frequency changes of the ICP. Representative analog processing may be used to measure the spacing between signal crossing above a certain thresh-
old (e.g. +/- 10-50 milli Gs). The time interval between the first two crossings may be indicative of the base line frequency. The shortest time interval between crossings may be indicative of the highest frequency. Digital signal processing could include the mathematical computations such as time-frequency transforms (See, e.g. "Time-frequency transforms: a new approach to first heart sound frequency dynamics", IEEE transactions in Biomedical Engineering, vol. 39, no. 7, July 1992) with peak frequency identification. Taking the mathematical derivative of the acceleration signal, analog or digital, would identify jerk motion. Measuring the jerk signals and the time difference between these signals could similarly characterize the frequency signal.

[0031] The output of the signal processing could be digital or analog and could be displayed on a workstation for graphical display of the ICP vibration. For example, an analog output would allow the signal to be input into a multi-channel electromogram recorder. The workstation used would typically have data storage and analysis capabilities. Alternatively a single number, such as the peak frequency or peak frequency divided by measured time interval, could be displayed. An accurate peak amplitude could be multiplied or divided by the time interval or frequency, or both multiplied and divided by the time interval or frequency, to yield a value related to LV function and improved response to therapies such as cardiac resynchronization therapy. Changes in this number would be used to guide the therapy and make changes such as the position of the LV pacing lead.

[0032] Devices and systems for incorporating acceleration sensors are described in the pending non-provisional patent application incorporated by reference above. The disclosed devices could be used to characterize the frequency dynamics of the ICP and pathologic LV vibration motion. Descriptions of exemplary devices are representative of acceleration sensing devices for the ICP and pathologic heart sounds.

[0033] An acceleration sensor may be incorporated into a catheter for insertion into the LV veins such as the coronary sinus, great cardiac veins, or tributary vessels of these veins. The acceleration sensor may also be incorporated into a probe inserted into the esophagus, which lies immediately behind the posterior surface of the heart. The acceleration sensor may be a single dual axis sensor oriented perpendicularly to the long axis of the catheter. This orientation of the sensor allows the measurement of longitudinal and radial acceleration signals, which predominate in the heart, from the coronary sinus and great cardiac vein. The catheter probe may have a guidewire lumen; however this may not be required for an esophageal probe. The catheter or esophageal probe may monitor the frequency dynamics of the ICP and assess LV function. The esophageal probe could be used to monitor the ICP and third and fourth heart sounds to detect ischemia, for example during surgical procedures. For example, a decrease in amplitude of the ICP signal as measured by the esophageal probe could be indicative of ischemia. Because the esophageal probe would not move with heart contraction and the patient would be static during surgery, more accurate amplitude measures could be obtained.

[0034] In addition the catheter and esophageal probe may be used to identify target LV pacing regions for CRT using a pacing guide wire. Referring to FIG. 4(A)-(E), a guide catheter 102 is shown with a proximal end 104. An acceleration sensing catheter 100, that may be inserted into the guide catheter 102, is shown with a pacing guidewire port 114 and a guidewire lumen 108. The guidewire lumen may have a diameter of, e.g., 0.014" to 0.038". The catheter 100 also has a sensor assembly 106 that may have one, two, or three acceleration sensors disposed within, the sensors being disposed perpendicularly to each other. The catheter 100 may have a bend near the distal end thereof, as shown in FIG. 4(B). The bend may be from 0 degrees to 90 degrees. At the proximal end of catheter 100 is also disposed a power source such as a battery 126, a connector for low frequency (<20 Hz) signals 124, a connector for mid-frequency (20 Hz to 150 Hz) signals 122, and a connector for high frequency (>150 Hz) signals 118.

[0035] A pacing guidewire 120 is shown in FIG. 4(C) having an insulated region 128 and an uninsulated region 132 for pacing. A flexible conductor 134 is disposed at the proximal portion of the guidewire 120, as well as a connector 136 to a pulse generator.

[0036] FIG. 4(D) shows a more detailed view of the catheter 100, showing the guide lumen 108 and an alternate sensor assembly 112. The sensor assembly 112 is perpendicular to the long axis of the catheter 100.

[0037] Referring to FIG. 4(E), the mapping system 710 is made of an acceleration sensing catheter 700 and a pacing guidewire 684. The pacing guidewire may be powered by a pulse generator 712.

[0038] The output of the sensors may be connected to a signal conditioning module and battery power module 714 prior to input into the electromogram recording 716 and display device 718. The output of the signal conditioning module may be analog signals if the electromogram signal is to be used. The signal conditioning module may also be used to correct or zero out the effects of gravity and the related tilt signal. Output from the signal conditioning module may also be digital. A microprocessing chip in the conditioning module may also perform functions such as forming a composite signal from multiple orientation axes and integration. The catheter within the guide catheter may have a guidewire lumen through which a pacing guidewire may be used to test pace target sites. This catheter may also have a port for contrast injection and may additionally have a balloon to perform an occlusive venogram.

[0039] A pacing guidewire would be positioned in various regions of the LV veins to elicit contractions. The LV response to this pacing may be measured by monitoring the frequency dynamics of the vibrational motion during ICP with the catheter. FIG. 5 indicates this technique. In particular, the figure shows improved myocardial function post-stimulation as determined by an increase in the peak frequency of the isovolumetric contraction phase. The left side of FIG. 5 shows the post-stimulation signal, and the right side shows the pre-stimulation signal. As can be seen, the peak frequency increases post-stimulation from about 80 Hz to about 170 Hz (note that the peak frequency is related to the time interval of the threshold crossing). Also seen is a shortening of the time interval of the isovolumetric contraction phase from about 100 ms to about 75 ms. The isovolumic contraction phase signal was acquired by sampling over a 100 ms time period after the onset of the QRS ECG signal.

[0040] Alternatively the frequency dynamics or amplitude could be measured with the esophageal probe. LV regions
associated with changes in the ICP frequency indicative of improved LV function would be target pacing regions. For example, an increase in the peak frequency, the rate of change of the frequency over time, a reduction in the baseline frequency, or some combination of the three may be indicative of improved LV function. Similarly, the location of implantation and pacing of the RV lead or right atrial lead may also be optimized by test pacing and monitoring the frequency dynamics of the ICP.

[0041] The change in the presence or frequency of the third or fourth heart sounds may also be indicative of a favorable response to pacing and hence help identify a target pacing region. Changes in the frequency and duration of vibration motion related to mitral valve regurgitation may also help guide therapy and target pacing regions. Thus a reduction in the frequency or duration of the signal may be indicative of a favorable response.

[0042] In more detail, referring to FIG. 6, which shows myocardial motion mapping, display output, and target pacing identification through a roving pace guidewire, changes or variables indicative of a favorable LV functional response may be sensed at the low, mid, and high frequency ranges. In the figure, “MVR” refers to mitral valve regurgitation, “IVC” refers to isovolumic contraction, and “IVR” refers to isovolumic relaxation. The top curve is ECG 556, curve 558 shows the velocity or LV displacement, obtained by integrating the acceleration signal, curve 562 shows LV function, and curve 562 shows the sounds of mitral valve regurgitation.

[0043] ECG 556 shows the QRS and T waves along with a pacing spike 560 which is delivered in the LV vein region. Examination of curve 558 shows a delayed onset motion 560 but a lessened delayed onset motion 571 following the pacing spike. Curve 562 shows a value of ejection phase 574, as measured by the time between the MVC or IVC and the AVC or IVR, and then a longer ejection phase 576. Here the MPI can be seen to be MPl=(a+b)/c. Curve 564 shows a reduced MVR signal 578 as compared to the pre-pacing MVR signal 582. Finally, it is noted that paced signal shows no third heart sound.

[0044] The accelerometer for monitoring the frequency dynamics of heart sounds may also be integrated into a pulse generator of a CRT/defibrillator device, including leadless defibrillator devices implanted subcutaneously over the chest. This device would be implanted subcutaneously on the chest or abdomen and would sense the vibrational motion of the heart sounds (S1, S2, S3, S4 and valvular murmurs) to characterize the peak amplitude and frequency. This pulse generator could perform software algorithms to characterize the frequency dynamics of these sounds and assess LV function and pathology including contractility, mitral regurgitation, LV thickening etc. The start of systole as measured by the cardiac electrogram (internally or externally measured by the IPG) could be used to synchronize the accelerometer sensor with the onset of systole. Thus the S1 vibrational motion as measured by the accelerometer would occur within a few milliseconds of the sensed electrogram. Thereafter, additional vibrational motion (S2, S3, and S4 and murmurs) could be identified based on their occurrence after the electrogram and S1. Additional a time window of sensing with the acceleration sensor (e.g. 100 ms) could be sensed to measure only the S1. With the This information could be uploaded via a radiofrequency link to provide a read out to the physician for monitoring purposes. The RF communication device that would acquire the data from the pulse generator could reside at the patients home and be transmitted to a physician or central monitoring station via the internet or a phone line link. The accelerometer could also be used to sense that the patient in whom the device is implanted is not moving and is in the proper orientation (e.g. upright or lying flat) prior to the acquisition of the heart function data.

[0045] A stand alone implantable accelerometer device (IAD) (i.e. not incorporated into the IPG/CRT device) could be implanted subcutaneously or subpectorally and not require a transvenous lead or extension. For example, referring to FIG. 7(B), a subpectorally placed IAD 208 may be disposed adjacent the pectoral muscle 210 of a patient. The device 208 may have an acceleration sensor 220, an RF communications transceiver chip 214 and antenna 212, signal processing and control circuit 218 with digital memory storage capacity 222, and a battery 216. Referring to FIG. 7(A), the device 208 may be contained in a hermetically sealed titanium shell 202. The device could have a curved form factor as shown in FIG. 7(A) to lie flat along the chest. The antenna could be wire wound or integrated onto the communications chip. The sensor may be a low-power consumption 3-axis MEMs device. The device may sense at a frequency greater than about 20 Hz to avoid acceleration signals due to respiration or displacement motion of the heart. Optional electrodes 204 and 206 with accompanying circuitry may be employed to obtain a surface cardiac electrogram. As shown in FIG. 7(A), the electrodes would reside on the side of the device that is oriented toward the heart. 3-7 years of battery life may be provided, although variations are within the scope of the invention. Low power RF transceiver chips (applications specific integrated circuit or ASIC), such as that produced by Zarlax Semiconductor of San Diego, Calif. (e.g., model number ZL 70100) can improve battery life and data transmission of the device. The device need not require leads that extend into the heart and may reside in proximity to the left ventricle after subcutaneous or subpectoral implantation. The device may sense and measure vibrational data related to LV function and pathology such as frequency dynamics, time intervals, and peak amplitude of the ICP, S1, S2, S3, S4, and valvular murmurs. The surface of the device oriented toward the heart may have electrodes for sensing the surface electrocardiogram and the onset of the QRS. Similar to the inventor’s prior applications, incorporated by reference above, this allows for the identification of the S1 as the vibrational signal immediately following the QRS. The subsequent vibrational signals could also be identified and time windows of sensing could also be incorporated to focus on the desired heart sound/vibrational motion. A narrow window of sensing that ascertains only the S1 vibrational signal may be preferred to avoid signal distortion or noise caused by movement of the heart against the chest during displacement or ejection. The S1 may be sensed and averaged over several to many beats. The vibrational motion could be sensed continuously or periodically. Periodic sensing may be used to extend battery life. The data may be collected at the same time during each day (e.g., at bedtime during quiet resting). The acceleration data could be stored or uploaded via an RF link in real time. The accelerometer could be battery-powered or inductively-powered with an
RF coil. The data could be periodically or in real time uploaded with an RF link to a signal processing station for monitoring of the LV function such as contractility and pathology such as LV mass/thickness and valvular murmurs. The uploaded data could be sent via the internet to a physician or central monitoring station or both. The device could also interface with a cell phone type device for the same purpose of uploading data from the IAD.

[0046] Analysis of the frequency dynamics of the ICP (catheter or esophageal probe) could also be used to optimize the pacing timing intervals for CRT (A-V and V-V). Thus the V-V timing could be set to 0 ms (both ventricles paced simultaneously), and the A-V delay could be varied between about 100 and 140 ms. The AV delay that provides the highest peak frequency (or some other measure of improved cardiac function) during ICP could be chosen. Subsequently the A-V delay would be fixed at the previously determined optimal value and the V-V delay could be varied between +30 ms (LV to RV; thus +30 means the RV was paced 30 ms before the LV) to +30 ms LV to RV. Again the interval causing the highest peak frequency during ICP may be chosen. An automated system could run through the various pacing timing intervals and monitor the frequency dynamics of the ICP and provide optimal timing intervals.

[0047] The acceleration sensor may also be incorporated into the lead of a CRT or CCM device. The sensor may monitor the frequency dynamics of the ICP to ascertain cardiac function in a manner similar to the above. The sensor could also be used to test different timing intervals for the atrioventricular and interventricular timing. The sensor may also be integrated into other implantable devices such as cardiac stents or epicardial leads to monitor cardiac function through analysis of the frequency dynamics of the ICP and pathologic heart sounds.

[0048] FIG. 8 shows how information from the acceleration sensor can be employed to develop a predictive algorithm for determining CRT response. The peak amplitude and peak frequency are seen at LV site #3. A linear threshold relationship, or other such relationship, may be employed to determine when LV lead placement is acceptable for any given patient. If the amplitude is high enough at a certain frequency, and thus is above the linear threshold, then the response may be deemed to be good and the site chosen as a location for an LV lead.

[0049] The invention has been described with respect to certain embodiments. It will be clear to one of ordinary skill in the art given this disclosure that variations may be made to these embodiments. Accordingly, the scope of the invention is to be limited only by the claims appended hereto.

1. A system for monitoring cardiac function, comprising:
   - a catheter component, the catheter component including:
     - a portion for insertion within or on a patient's heart, the insertion portion including an acceleration sensor;
     - an external portion including a connector to carry signals from the acceleration sensor;
     - a signal receiving and analysis component, the signal receiving and analysis component including:
       - a frequency analyzer to analyze the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor.
   - The device of claim 1, wherein the sensor measures acceleration in three perpendicular components.
   - The device of claim 1, wherein the frequency analyzer analyzes the frequency dynamics of the S1 heart sound as well as the frequency dynamics of at least one other heart sound.
   - The device of claim 1, wherein the sensor is synchronized with a cardiac electrical signal indicative of the onset of myocardial contraction.
   - The device of claim 1, wherein the cardiac function monitored is heart failure.
   - The device of claim 1, wherein the frequencies analyzed are greater than about 20 Hz.
   - The device of claim 4, further comprising an ECG component to measure an ECG of the patient, and wherein the sensor is synchronized with the R-wave measured by the ECG.
   - The device of claim 7, wherein the signal receiving and analysis component further comprises a circuit implemented in hardware, software, firmware, or a combination of the above, to analyze the frequency change of the signal measured by the sensor.
   - A method for monitoring cardiac function, comprising:
     - inserting a catheter into a patient, a distal tip of the catheter including a section that resides within or on a patient's heart, the section including an acceleration sensor;
     - receiving signals from the acceleration sensor at a signal receiving and analysis component;
     - analyzing the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor.
   - The method of claim 9, further comprising analyzing the frequency dynamics of at least one other heart sound besides the S1.
   - The method of claim 9, wherein the cardiac function monitored is heart failure.
   - A system for optimizing CRT lead placement and/or CRT device timing intervals, comprising:
     - a test pacing component to perform test pacing of a patient's heart;
     - a catheter component, the catheter component including:
       - a portion for insertion within or on a patient's heart, the insertion portion including an acceleration sensor to monitor heart sounds responding to the test pacing;
       - an external portion including a connector to carry signals from the acceleration sensor;
       - a signal receiving and analysis component, the signal receiving and analysis component including:
         - a frequency analyzer to analyze the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor in response to the test pacing.
   - The system of claim 12, wherein the sensor measures acceleration in three perpendicular components.
14. The system of claim 12, wherein the frequency analyzer analyzes the frequency dynamics of the S1 heart sound as well as the frequency dynamics of at least one other heart sound.

15. The system of claim 12, wherein the sensor is synchronized with a pacing spike from the test pacing component.

16. The system of claim 14, wherein the frequencies analyzed include those at frequencies greater than about 20 Hz.

17. The system of claim 12, wherein the test pacing component is a pacing guidewire.

18. A method for optimizing CRT lead placement and/or CRT device timing intervals, comprising:

- inserting a catheter into a patient, a distal tip of the catheter including a section that resides within or on a patient’s heart, the section including an acceleration sensor;
- inserting a test pacing component within or on a patient’s heart;
- receiving signals from the acceleration sensor at a signal receiving and analysis component in response to the test pacing;
- analyzing the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor in response to the test pacing.

19. The method of claim 18, further comprising analyzing the frequency dynamics of at least one other heart sound besides the S1.

20. A system for monitoring cardiac function, comprising:

- an implantable component, the implantable component including an acceleration sensor and a transmitter;
- a signal receiving and analysis component, the signal receiving and analysis component including:
  - a receiver to receive signals from the transmitter; and
  - a frequency analyzer to analyze the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor.

21. The system of claim 20, wherein the sensor measures acceleration in three perpendicular components.

22. The system of claim 20, wherein the receiver is a wand-type receiver.

23. The system of claim 20, wherein the implantable component further comprises a rechargeable battery and wherein the signal receiving and analysis component further comprises a wireless battery charger for recharging the battery.

24. The system of claim 20, wherein the frequency analyzer analyzes the frequency dynamics of the S1 heart sound as well as the frequency dynamics of at least one other heart sound.

25. A method for monitoring cardiac function, comprising:

- subcutaneously inserting an implantable component into a patient, the implantable component including an acceleration sensor and a transmitter;
- receiving signals from the acceleration sensor at a signal receiving and analysis component;
- synchronizing the acceleration sensor with a signal received from the surface electrode corresponding to the onset of myocardial contraction;
- analyzing the frequency dynamics of at least the S1 heart sound as measured by the acceleration sensor.

26. The method of claim 25, further comprising analyzing the frequency dynamics of at least one other heart sound besides the S1.

27. The method of claim 25, wherein the frequencies analyzed are greater than about 20 Hz.

28. A system for long-term monitoring of heart failure, comprising:

- a housing, including:
  - an accelerometer;
  - a transceiver chip coupled to the accelerometer;
  - a battery coupled to the accelerometer;
- wherein said housing is structured and configured to be implanted subcutaneously to monitor vibrational motion of the heart.

29. The system of claim 28, further comprising at least one surface electrode structured within or on the housing for sensing a surface ECG.

30. The system of claim 28, wherein the housing is integrated into a CRT device.

31. The system of claim 28, wherein the housing is integrated into an implantable defibrillator.

32. The system of claim 31, wherein the housing is integrated into a leadless implantable defibrillator.

33. The system of claim 29, wherein the accelerometer senses vibrational motion in a time window of 100 milliseconds or less following a QRS of the surface ECG.

34. A method for monitoring cardiac function, comprising:

- installing an acceleration sensor within or on a patient’s heart;
- installing a surface ECG electrode and measuring a patient’s surface ECG; and
- sensing vibrational motion in a time window following the R-wave measured by the surface ECG.

35. The method of claim 34, wherein the sensing further comprises sensing acceleration in three perpendicular components.

36. The method of claim 34, wherein the sensing is at a frequency greater than about 20 Hz.

37. The method of claim 34, wherein the sensing further comprises sensing vibrational motion in a time window of 100 milliseconds or less following a QRS of the surface ECG.

38. The method of claim 34, wherein the acceleration sensor and the surface ECG electrode are disposed within a single housing.

39. A method for optimizing CRT device timing intervals, comprising:

- test pacing a patient’s heart;
- monitoring heart sounds responding to the test pacing using an acceleration sensor;
receiving signals corresponding to the monitored heart sounds;

analyzing the frequency dynamics of the received signals;

varying an AV or VV timing interval of the test pacing while analyzing the changes of the varying on the frequency dynamics.

40. The method of claim 39, wherein the test pacing includes test pacing with a pacing guidewire.

41. The method of claim 39, wherein the acceleration sensor is mounted on a catheter.

42. The method of claim 39, wherein the receiving signals includes receiving signals including at least the S1 heart sound.

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