



US010039468B2

(12) **United States Patent**
Gupta et al.

(10) **Patent No.: US 10,039,468 B2**
(45) **Date of Patent: Aug. 7, 2018**

(54) **NONINVASIVE ELECTROCARDIOGRAPHIC METHOD FOR ESTIMATING MAMMALIAN CARDIAC CHAMBER SIZE AND MECHANICAL FUNCTION**

(71) Applicant: **Analytics For Life**, Ganaoque (CA)

(72) Inventors: **Sunny Gupta**, Amherstview (CA);
Timothy William Fawcett Burton,
Ottawa (CA); **Shyamlal Ramchandani**,
Kingston (CA); **Derek Vincent Exner**,
Calgary (CA)

(73) Assignee: **Analytics For Life Inc.**, Toronto,
Ontario (CA)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/077,993**

(22) Filed: **Nov. 12, 2013**

(65) **Prior Publication Data**

US 2015/0133803 A1 May 14, 2015

(51) **Int. Cl.**
A61B 5/04 (2006.01)
A61B 5/0452 (2006.01)
A61B 5/00 (2006.01)

(52) **U.S. Cl.**
CPC **A61B 5/0452** (2013.01); **A61B 5/04011**
(2013.01); **A61B 5/7275** (2013.01); **A61B**
2576/023 (2013.01)

(58) **Field of Classification Search**
CPC . A61B 2019/5295; A61B 5/0073; A61B 5/04;
A61B 5/0402; A61B 5/044; A61B
5/0452; A61B 6/466; A61B 6/5211; A61B
6/5217; A61B 6/5229; A61B 8/466

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2003/0083586 A1 5/2003 Ferek-Petric
2008/0114257 A1* 5/2008 Molin A61B 5/04011
600/512
2010/0217144 A1 8/2010 Brian
(Continued)

OTHER PUBLICATIONS

Bellenger, N.G., et al., "Comparison of left ventricular ejection fraction and volumes in heart failure by echocardiography, radionuclide ventriculography and cardiovascular magnetic resonance: Are they interchangeable?", European Heart Journal, vol. 21, No. 16, 2000, pp. 1387-1396.

(Continued)

Primary Examiner — Christopher D Koharski

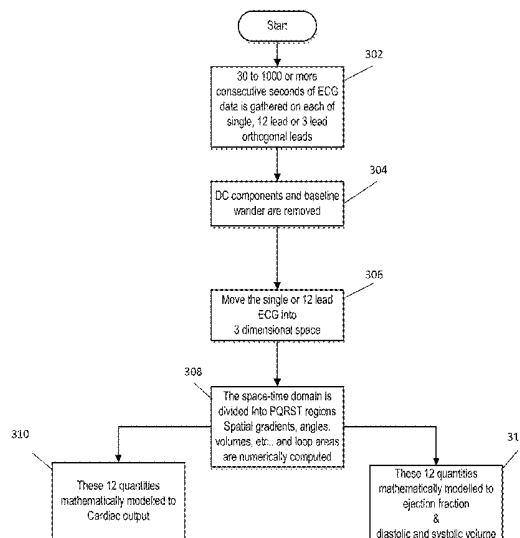
Assistant Examiner — Elizabeth K So

(74) *Attorney, Agent, or Firm* — Meunier Carlin &
Curfman LLC

(57) **ABSTRACT**

The present disclosure generally relates to systems and method of a noninvasive electrocardiographic (ECG) technique for characterizing cardiac chamber size and cardiac mechanical function. A mathematical analysis of three-dimensional (3D) high resolution ECG data may be used to estimate chamber size and cardiac mechanical function. For example, high-resolution mammalian ECG signals are analyzed across multiple leads, as 3D orthogonal (X,Y,Z) or 10-channel data for 30 to 1400 seconds to derive estimates of cardiac chamber size and cardiac mechanical function. Multiple mathematical approaches may be used to analyze the dynamical and geometrical properties of the ECG data.

7 Claims, 4 Drawing Sheets



(56)

References Cited

U.S. PATENT DOCUMENTS

2011/0251504 A1* 10/2011 Tereshchenko A61B 5/04011
600/512
2013/0096394 A1* 4/2013 Gupta A61B 5/04012
600/301
2014/0194758 A1 7/2014 Korenberg
2014/0207005 A1 7/2014 Bukkapatnam et al.

OTHER PUBLICATIONS

Edenbrandt, L., "Vectorcardiogram Synthesized From a 12-lead ECG: Superiority of the Inverse Dower Matrix," *Journal of Electrocardiography*, vol. 21, No. 4, 1988, pp. 361-367.
"Ejection Fraction" from Wikipedia. http://en.wikipedia.org/wiki/Ejection_fraction, last accessed Mar. 25, 2016, 5 pages.
Fioretti, P., et al., "Limitations of a QRS scoring system to assess left ventricular function and prognosis at hospital discharge after myocardial infarction," *Br Heart J.*, vol. 53, No. 3, 1985, pp. 248-252.
Gholamrezanezhad, A., et al., "A correlative study comparing current different methods of calculating left ventricular ejection fraction," *Nuclear Medicine Commun.*, vol. 28, No. 1, 2007, pp. 41-48.

Jaarsma, C., et al., "Comparison of Different Electrocardiographic Scoring Systems for Detection of any Previous Myocardial Infarction as Assessed With Cardiovascular Magnetic Resonance Imaging," *American Journal of Cardiology*, vol. 112, No. 8, 2013, pp. 1069-1074.

Mikell, F.L., et al., "Reliability of Q-wave formation and QRS score in predicting regional and global left ventricular performance in acute myocardial infarction with successful reperfusion," *American Journal of Cardiology*, vol. 57, No. 11, 1986, pp. 923-926.

Murkofsky, R.L., et al., "A Prolonged QRS Duration on Surface Electrocardiogram Is a Specific Indicator of Left Ventricular Dysfunction," *Journal of the American College of Cardiology*, vol. 32, No. 2, 1998, pp. 476-482.

Nikitin, N.P., et al., "New generation 3-dimensional echocardiography for left ventricular volumetric and functional measurements: comparison with cardiac magnetic resonance," *European Journal Echocardiography*, vol. 7, No. 5, 2006, pp. 365-372.

Palmeri, S.T., et al., "A QRS scoring system for assessing left ventricular function after myocardial infarction," *New England Journal of Medicine*, vol. 306, No. 1, 1982, pp. 4-9.

Wagner, G.S., et al., "Evaluation of a QRS Scoring System for Estimating Myocardial Infarct Size. I. Specificity and Observer Agreement," *Circulation*, vol. 65, No. 2, 1982, pp. 342-347.

* cited by examiner

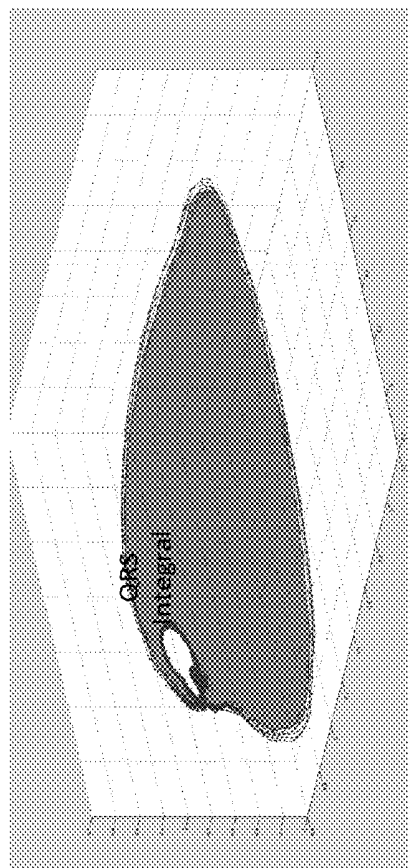
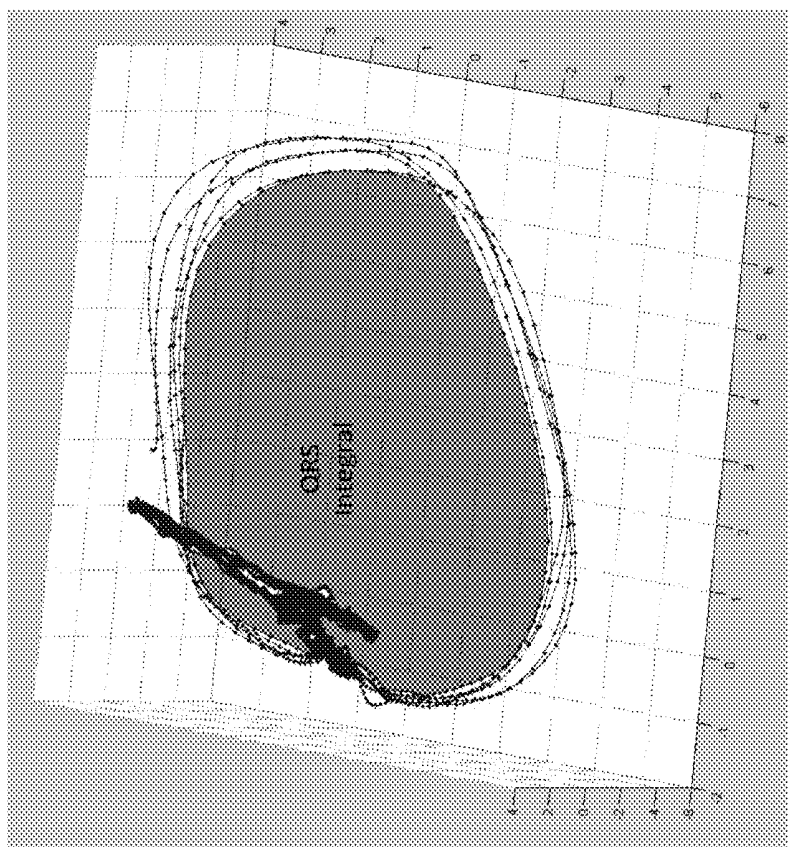


Fig 1

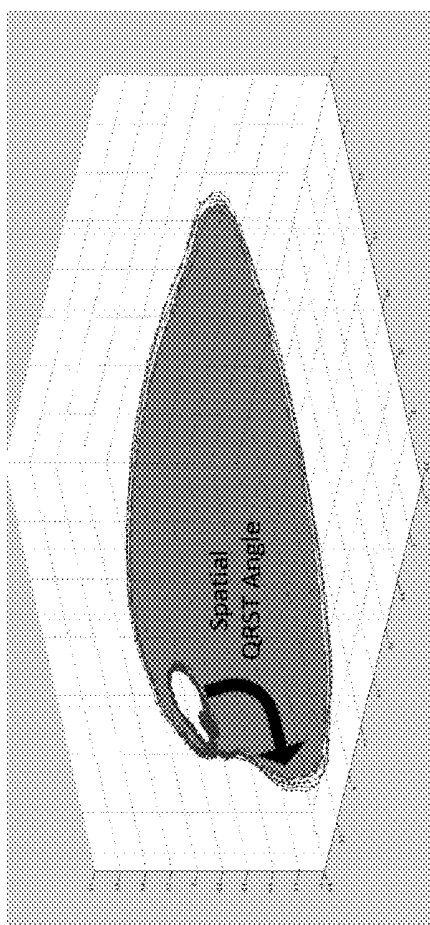
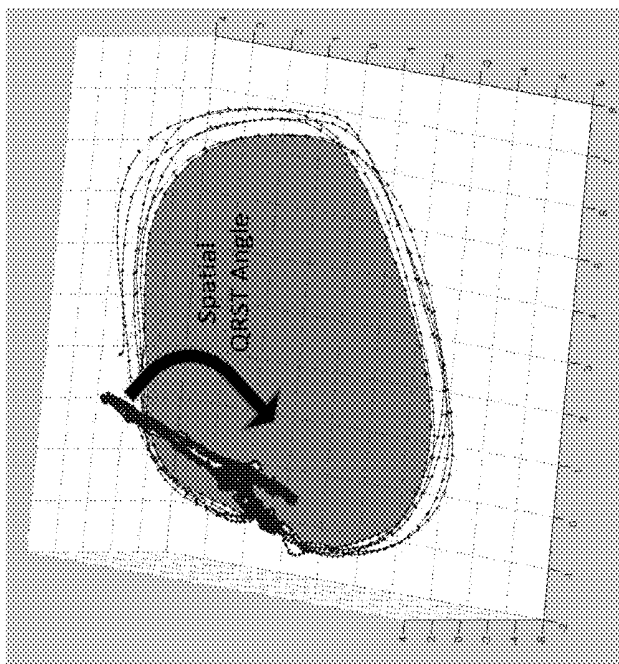
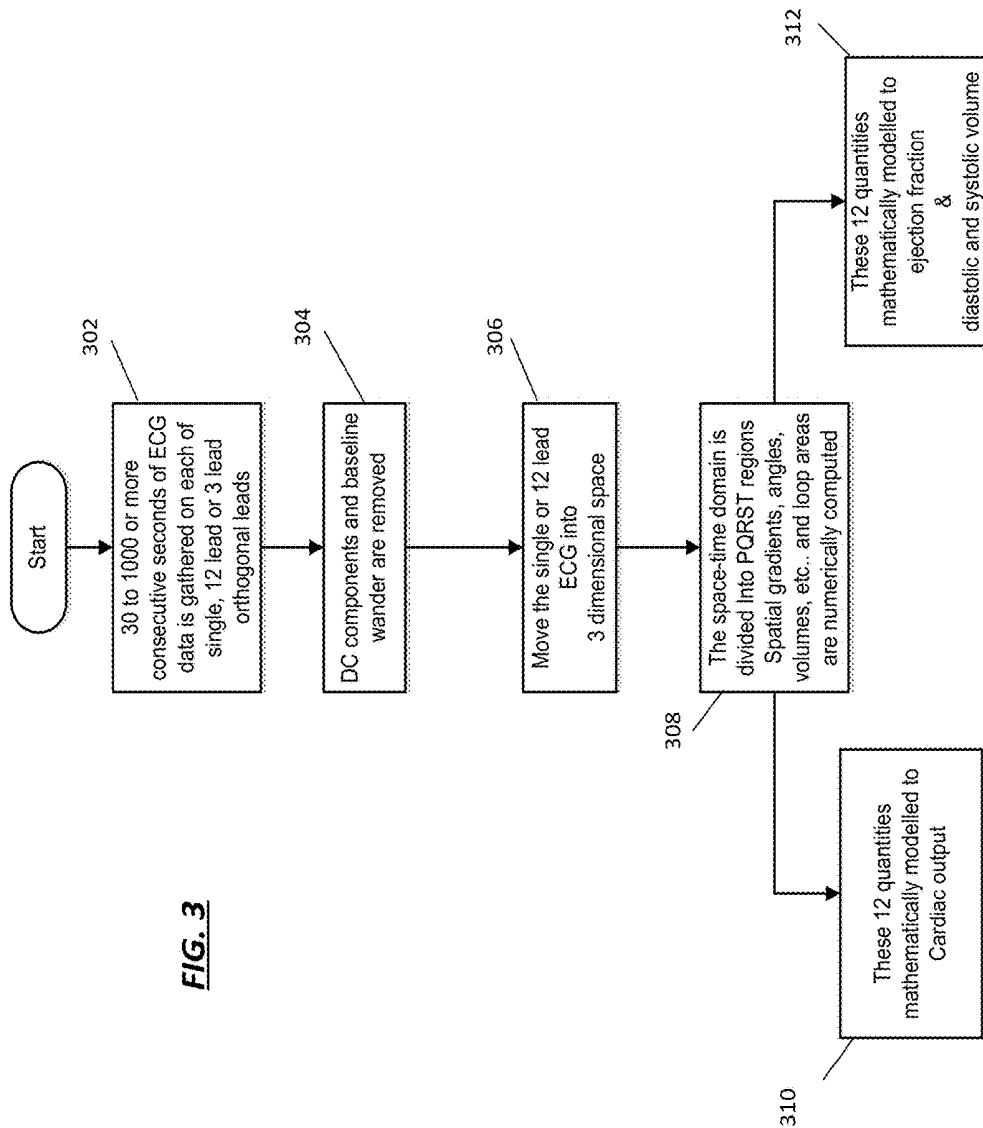


Fig 2



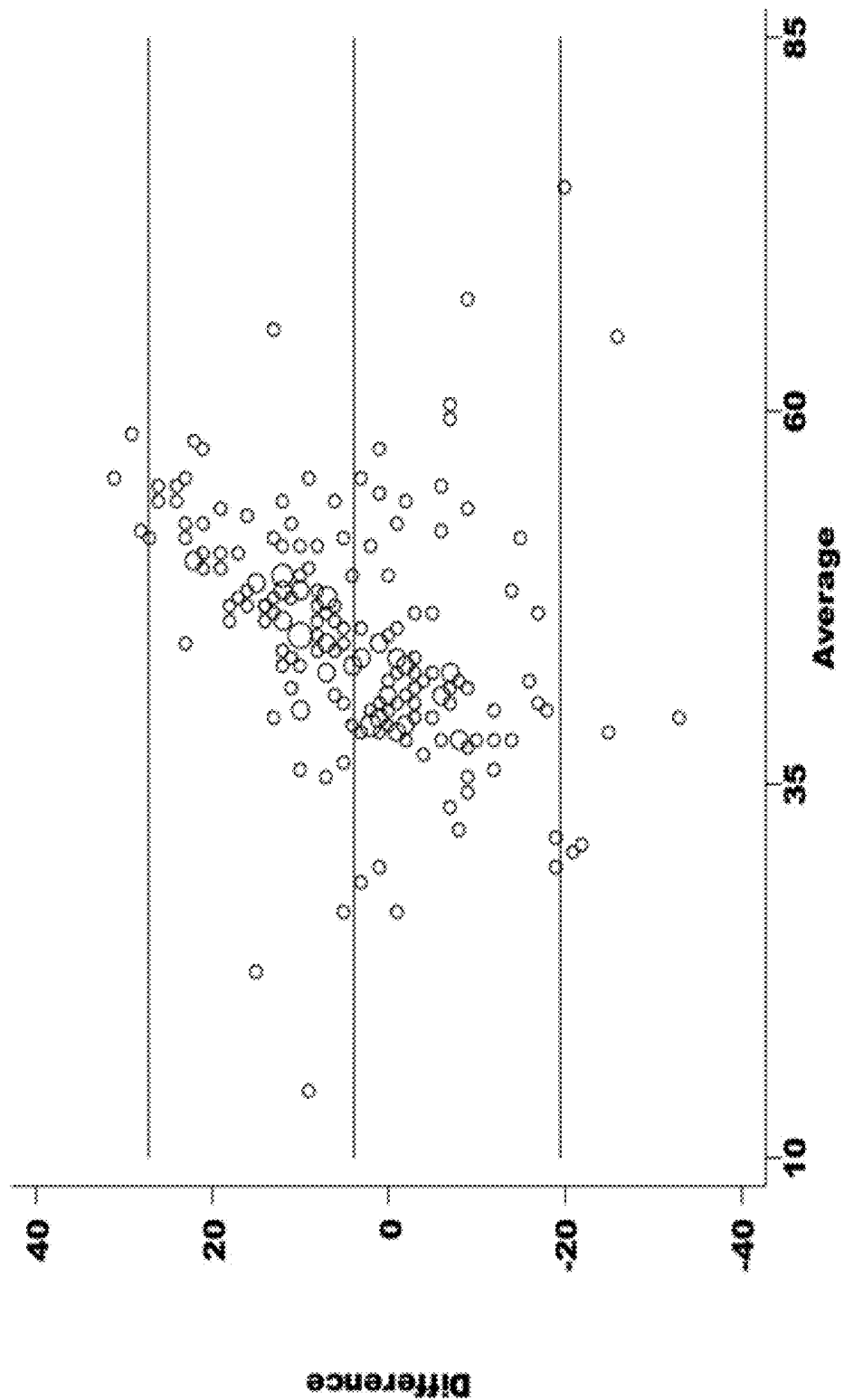


Fig 4

NONINVASIVE ELECTROCARDIOGRAPHIC METHOD FOR ESTIMATING MAMMALIAN CARDIAC CHAMBER SIZE AND MECHANICAL FUNCTION

BACKGROUND

A variety of measures of cardiac function are used in clinical practice. The formulae used in their calculations are (1):

$$\text{Stroke Volume (SV)} = \text{End Diastolic Volume (EDV)} - \text{End Systolic Volume (ESV)}$$

$$\text{Ejection Fraction (EF)} = (\text{SV} / \text{EDV}) \times 100\%$$

$$\text{Cardiac Output (Q)} = \text{SV} \times \text{Heart Rate (HR)}$$

Assessment of cardiac chamber size, including the left ventricle (LV), is commonly undertaken using cardiac ultrasound (echocardiography), radionuclide angiography (RNA), and cardiac magnetic resonance (CMR) imaging. Each technique measures the change in chamber size with each heartbeat; reflecting the amount of blood ejected with each heartbeat. These measures are then used to estimate cardiac mechanical function. The SV is the fraction of blood ejected with each heartbeat and EF is that fraction divided by the amount of blood at rest or in diastole; as measured using the end diastolic volume (EDV). Cardiac output (Q) reflects the volume of blood over time and is the product of SV multiplied by heart rate (HR).

Presently used techniques to estimate LVEF are costly, have limited access in many regions, and require interpretation by a clinician. Moreover, techniques that use radionuclide pharmaceuticals pose a risk to patients and healthcare providers in terms of radiation exposure. Further, there is generally poor correlation between these techniques in terms of the LVEF value obtained. Of the various techniques use, both CMR and RNA are considered to represent "gold standard" methods for assessing LVEF in terms of the value obtained and prognosis. Yet, studies comparing RNA with CMR have found only modest correlation ($r=0.87$) and significant rates of misclassification between these "gold standard" techniques. For example, a 10% or larger individual difference in LVEF was found in 23% of patients. (2). A technology that can reliably estimate LVEF from a common cardiovascular test that is noninvasive and can be readily implemented (i.e., an ECG) has tremendous clinician ideal.

Algorithms commonly employed in signal processing of cardiac signals are typically rudimentary. They can be improved upon using contemporary techniques that evaluate the detailed characteristics of high-resolution 3D ECG signals in terms of geometric relationships, conduction properties, and other characteristics.

The surface ECG contains detailed information on the electrical properties of the heart. A surface ECG signal represents the summation of the individual action potentials from each and every cardiac cell in syncytium. Hence, global alterations in the surface ECG would be expected to reflect the mechanical function of the heart. Moreover, information related to the conduction properties of myocardial tissue is inherent in the surface ECG. A major challenge is discrimination of the pertinent information from a long quasi-periodic ECG signal while excluding noise contamination.

There is a distinct lack of ECG based algorithms to estimate cardiac chamber size and cardiac mechanical func-

tion. Various metrics have been developed to estimate chamber enlargement and cardiac mechanical function. These include estimating chamber size based on the amplitude and duration of ECG features (e.g., left atrial abnormality), estimating cardiac mechanical function based on the presence or absence of Q waves, the presence or absence of prominent conduction delays, and the overall amplitude of ECG signals (e.g., QRS voltage). While each approach appeared promising during the development phase, none has been shown to be useful with independent validation in less select populations. (3-10) Yet, it is desirable for an ECG-based system and method to determine cardiac chamber size and systolic function (i.e., LVEF) due to the utility of this data in screening and for daily clinical decision-making. Moreover, these data have been shown to have important prognostic value.

SUMMARY OF THE DISCLOSURE

The present disclosure generally relates to a noninvasive electrocardiographic (ECG) method and technique for characterizing cardiac chamber size and cardiac mechanical function. Disclosed herein are methods that utilize mathematical analysis of three-dimensional (3D) high resolution ECG data to estimate chamber size and cardiac mechanical function. For example, high-resolution mammalian ECG signals are analyzed across multiple leads, as 3D orthogonal (X,Y,Z) or 10-channel data for 30 to 1400 seconds to derive estimates of cardiac chamber size and cardiac mechanical function. Multiple mathematical approaches may be used to analyze the dynamical and geometrical properties of the ECG data understudy.

In accordance with an aspect of the disclosure, there is a disclosed a noninvasive method for analyzing mammalian ECG signals to accurately estimate cardiac chamber size and cardiac mechanical function. The method includes obtaining 3D ECG data; processing the ECG data to noninvasively determine a cardiac chamber size; processing the ECG data to noninvasively estimate cardiac mechanical function; applying a model to measure at least one of a sum QRST integral, 3D ECG volume integral, spatial QRST angle, QRS loop volumes, T loop volumes, spatial ventricular gradient, spatial ventricular gradient, spatial ventricular gradient elevation and beat-to-beat variability in such values; and adjusting results of the model with clinical data to estimate cardiac chamber size and cardiac chamber mechanical function.

In accordance with other aspects, there is provided an ECG analysis system for analyzing ECG measurements obtained from a patient to determine a patient's cardiac chamber size and cardiac mechanical function corresponding to a level of risk of the patient experiencing a subsequent clinical event. The ECG analysis system may include a 3D ECG measuring component that obtains orthogonal or multi-lead ECG measurements and an ECG analysis component operatively connected to the ECG measuring component that receives the ECG measurements, performs an ECG analysis, and provides ECG analysis results in a user readable format. The ECG analysis includes determining at least one cardiac event risk factor having a value, the at least one cardiac event risk factor being determinable from a group of cardiac function values, cardiac output, stroke volume, end-diastolic volume, end-systolic volume and ejection fraction, and beat-to-beat variability in such values.

Other systems, methods, features and/or advantages will be or may become apparent to one with skill in the art upon examination of the following drawings and detailed descrip-

tion. It is intended that all such additional systems, methods, features and/or advantages be included within this description and be protected by the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

The components in the drawings are not necessarily to scale relative to each other. Like reference numerals designate corresponding parts throughout the several views.

FIG. 1 illustrates exemplar vectorcardiograms and three dimensional integrals that may be computed and used in estimating cardiac chamber size and mechanical function;

FIG. 2 illustrates a spatial QRST angle that may be used as a metric evaluating cardiac chamber size and mechanical function;

FIG. 3 illustrates a workflow to generate a model that is predictive of ejection fraction, diastolic volume and systolic volume; and

FIG. 4 illustrates a Bland-Altman plot of predicted LVEF from the ECG against the MUGA measured ejection frac-

DETAILED DESCRIPTION

The present disclosure has been designed to assess cardiac chamber size and cardiac mechanical function by evaluating the electrical activity of the heart. With reference to the equations below, the present disclosure provides a method whereby high-resolution mammalian ECG signals are analyzed across multiple leads, as 3D orthogonal (X,Y,Z) or 10-channel data for 30 to 1400 seconds (Eq. 1) to derive estimates of cardiac chamber size and cardiac mechanical function. Multiple mathematical approaches are used to analyze the dynamical and geometrical properties of the ECG data under study.

FIG. 1 illustrates exemplar vectorcardiograms and three dimensional integrals that may be computed and used in estimating cardiac chamber size and mechanical function. The first method uses vectorcardiography and topology to characterize the ECG manifestations of the cardiac repolarization and depolarization process. The vectorcardiogram (VCG) is a method that records in the three planes of space the electrical potential of the heart during the cardiac cycle. Chamber activation manifests as the P loop (atrial depolarization), a dominant high amplitude QRS loop (ventricular depolarization) and the T loop (ventricular depolarization) (Eq. 10), which result from the spatial temporal summation of multiple vectors of bioelectric potentials that originate in the heart during the cardiac cycle. The entirety of the cycle is known as the PQRST, and can be referenced in sub-cycles. The spatial electrical gradients (Eq. 4) embedded the electrical properties relate to the volume and the local properties of the chamber of interest. This includes bioelectric inhomogeneities and the physics of cardiac mechanical function.

FIG. 2 illustrates a spatial QRST angle that may be used as a metric evaluating cardiac chamber size and mechanical function. The spatial gradients obtained by the VCG can be measured in a variety of ways including the QRST integral (Eq. 2), which captures the peak amplitudes, the size of the QRS vector loop (Eq. 9) and the angles of depolarization and repolarization (Eqs. 5,6). The depolarization of the heart moves from the endocardium to the epicardium and this is captured in the QRS vector loop volume (Eq. 9) morphology. This rapid myocardial activation in early ventricular systole develops perfusion pressure. Maximal right and left pressure is reached before the beginning of the T wave. These pressure gradients embed cardiac function in the voltage spatial gradients (Eq. 4). The pressure in the endocardium is higher than in the epicardium this forces ven-

tricular myocytes to repolarize in the epicardium first. The unequal distribution of endocardial pressure throughout the ventricles delays the time the endocardium begins repolarize and this delay is correlated to cardiac output. These delays can be quantified with the volume QRST integral (Eq. 3) over an ECG signal across each of the three leads (X, Y, Z) in a give time period (typically 30-1400 seconds). The magnitude of this integral is predictive when extracting LV chamber size and estimating LVEF from the ECG.

Other features required to reliably assess LVEF include, but are not limited to, the morphology of the VCG loop, conduction velocity over the initial 50% of the QRS VCG (Eq 7), and spatial alterations in the QRST angle.

Corrections for body size (body mass index), gender, cardioactive medications, and variations in ECG lead placement are required to reliably assess LVEF.

The aforementioned techniques and approaches can also be used to assess the size and function if other chambers including the right and left atria and to quantify myocardial relaxation, commonly referred to as diastolic function.

FIG. 3 illustrates a workflow to generate a model that is predictive of ejection fraction, diastolic volume and systolic volume. At 302, 30 to 100 (or more) consecutive seconds of ECG data is gathered each of single 12 lead with 3 lead orthogonal leads. At 304, DC components and baseline wander are removed. This may be performed by using a modified moving average filter created for each lead. At 306, the single or 12 lead ECG data is moved into three-dimensional space. This may be performed, for example, using delayed phase space reconstruction or Dower. At 308, the space-time domain is divided into PQRST regions, spatial gradients, angles, volumes, etc. and loop areas are numerically computed. At 310, 12 quantities are mathematical model to cardiac output. Alternatively or additionally, 312, the 12 quantities are mathematical model to ejection fraction and diastolic and systolic volume. Thus, the workflow of FIG. 3 provides a method to model cardiac output, ejection fraction, and diastolic and systolic volume.

FIG. 4 illustrates a Bland-Altman plot of predicted LVEF from the ECG against the MUGA measured ejection fraction. The techniques described herein were applied to a dataset of 195 orthogonal high resolution (1000 Hz) ECGs with paired MUGA evaluated left ventricular ejection fractions. The ejection fraction could not be reliably quantified in 16 recordings (8 percent) due to limitations of the technique and these patients were excluded from the analysis. The Bland-Altman plot was created to examine the disparity between the two measurements in the 195 patients in whom EF was reliably quantified by ECG. The mean difference between the two measurements was 4%, with a confidence interval of 2% to 6%. The range of the MUGA calculated ejection fraction values was 15% to 75%. The equation that combined the different characterization methods discussed to create these results is below. This exemplar is not limiting and there are other solutions in this family with similar diagnostic ability.

$$\begin{aligned} \text{Ejection} \\ \text{Fraction} = & \text{spatialVentricularGradientAzimuth} + \\ & \text{TWaveLoopVolume}^2 + 36.63895238712 * \text{erf} \\ & (1.29854235984933 + \\ & \text{spatialVentricularGradientAzimuth} * \text{QRVelocity} - \\ & \text{TWaveLoopVolume}) + \\ & (3.73595220608718 * \text{spatialConductionVelocityGradient} - 4.95 \\ & 485967820254 * \text{spatialVentricularGradientEleva-} \\ & \text{tion}) / (\text{TWaveLoopVolume}^2 + \text{erf}(\text{spatialVentricu-} \\ & \text{larGradient}^4 / (3.73595220608718 * \text{spatialCon-} \\ & \text{ductionVelocityGradient} - \\ & 4.95485967820254 * \text{spatialVentricularGradientElevation}))) + \text{CF} \end{aligned}$$

7

Having thus described implementations of the claimed invention, it will be rather apparent to those skilled in the art that the foregoing detailed disclosure is intended to be presented by way of example only, and is not limiting. Many advantages for non-invasive method and system for estimate cardiac chamber size and cardiac mechanical function have been discussed herein. Various alterations, improvements, and modifications will occur and are intended to those skilled in the art, though not expressly stated herein. Any alterations, improvements, and modifications are intended to be suggested hereby, and are within the spirit and the scope of the claimed invention. Additionally, the recited order of the processing elements or sequences, or the use of numbers, letters, or other designations therefore, is not intended to limit the claimed processes to any order except as may be specified in the claims. Accordingly, the claimed invention is limited only by the following claims and equivalents thereto.

What is claimed is:

1. An ECG analysis system for analyzing ECG measurements obtained from a patient to determine a patient's cardiac chamber size and cardiac mechanical function corresponding to a level of risk of the patient experiencing a subsequent clinical event, the ECG analysis system comprising:

a 3D ECG measuring component that obtains orthogonal or multi-lead ECG measurements; and

an ECG analysis component operatively connected to the ECG measuring component that receives the ECG measurements, performs an ECG analysis, and provides ECG analysis results to a user,

wherein the ECG analysis includes transforming the ECG orthogonal or multi-lead ECG measurements into three-dimensional space using phase space reconstruction

8

tion to mathematically derive at least one mechanical cardiac function from a set of mechanical cardiac functions including cardiac output, diastolic volume, systolic volume and ejection fraction.

2. The ECG analysis system of claim 1, wherein the ECG analysis results include a cardiac event risk factor of low, intermediate, or high based upon the value of the at least one cardiac event risk factor.

3. The ECG analysis system of claim 1, wherein ECG analysis component creates a VCG from the ECG data, and wherein ECG analysis component uses the 12 or N dimensional phase space diagram to determine cardiac chamber size and cardiac mechanical function.

4. The ECG analysis system of claim 1, wherein the ECG measurement component determines a cardiac chamber mechanical function by plotting a phase space PQRST curve for the ECG measurements, and wherein the ECG measuring component computes a sum QRS integral, 3DE CG volume integral, spatial QRS angle, QRS loop volumes, T loop volumes, spatial ventricular gradient, spatial ventricular gradient elevation and beat-to-beat variability in such values.

5. The ECG analysis system of claim 1, wherein a determination of cardiac chamber mechanical function is determined by computing the cardiac output, stroke volume, end-diastolic volume, end-systolic volume and ejection fraction.

6. The ECG analysis system of claim 5, wherein the 3D ECG data is measured over a number of beats or selected time period from 30 to 1400 seconds.

7. The ECG analysis system of claim 6, wherein a ventricular cardiac mechanical function is used to screen patients for structural heart disease.

* * * * *

专利名称(译)	用于估计哺乳动物心腔大小和机械功能的无创心电图方法		
公开(公告)号	US10039468	公开(公告)日	2018-08-07
申请号	US14/077993	申请日	2013-11-12
[标]申请(专利权)人(译)	ANALYTICS FOR LIFE		
申请(专利权)人(译)	ANALYTICS FOR LIFE		
当前申请(专利权)人(译)	ANALYTICS FOR LIFE INC.		
[标]发明人	GUPTA SUNNY BURTON TIMOTHY WILLIAM FAWCETT RAMCHANDANI SHYAMLAL EXNER DEREK VINCENT		
发明人	GUPTA, SUNNY BURTON, TIMOTHY WILLIAM FAWCETT RAMCHANDANI, SHYAMLAL EXNER, DEREK VINCENT		
IPC分类号	A61B5/04 A61B5/00 A61B5/0452		
CPC分类号	A61B5/0452 A61B5/7275 A61B5/04011 A61B2576/023		
其他公开文献	US20150133803A1		
外部链接	Espacenet		

摘要(译)

本公开一般涉及用于表征心腔尺寸和心脏机械功能的非侵入性心电图 (ECG) 技术的系统和方法。可以使用三维 (3D) 高分辨率ECG数据的数学分析来估计腔室尺寸和心脏机械功能。例如，跨多个导联分析高分辨率哺乳动物ECG信号，作为3D正交 (X , Y , Z) 或10通道数据30至1400秒，以得出心室大小和心脏机械功能的估计。可以使用多种数学方法来分析ECG数据的动态和几何特性。

