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(54) Title: METHOD AND SYSTEM FOR USE IN MONITORING LEFT VENTRICULAR DYSFUNCTION
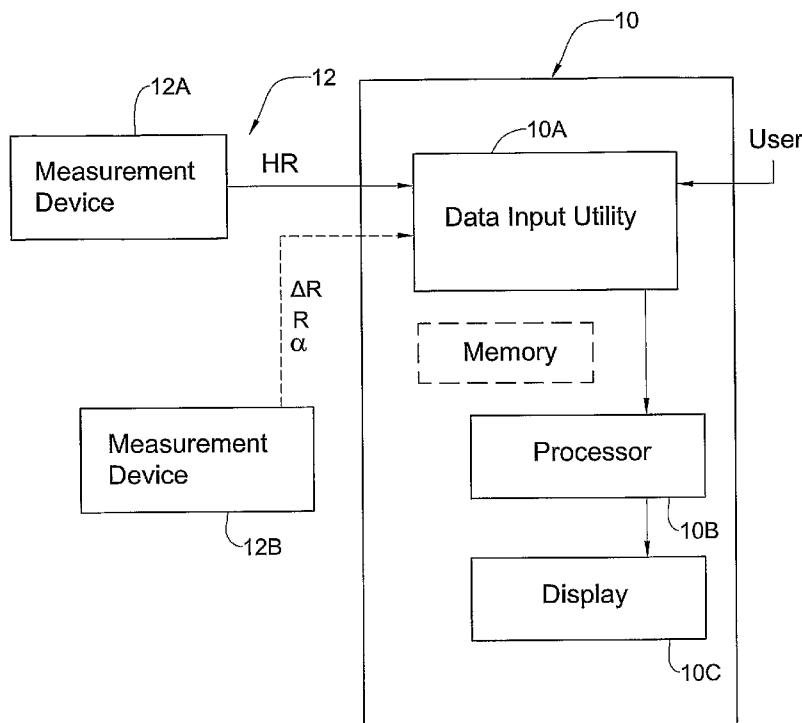
(57) **Abstract**: A method and system are presented for use in determining a patient's heart condition. First and second data are provided, where the first data is indicative of the patient's heart rate, and the second data is indicative of bioimpedance peak value during a cardiac cycle. A relation between a certain predetermined value and a product of the first and said second data is determined, where such relation is indicative of the patient's left ventricular condition, enabling to identify a left ventricular dysfunction.

FIG. 1

MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR),
OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG).

- 1 -

METHOD AND SYSTEM FOR USE IN MONITORING LEFT
VENTRICULAR DYSFUNCTION

FIELD OF THE INVENTION

The present invention is generally in the field of bioimpedance based monitoring techniques, and relates to a method and system for monitoring a patient's condition aimed at determining left ventricular dysfunction.

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BACKGROUND OF THE INVENTION

Congestive heart failure (CHF) is most commonly associated with dilated left ventricle (LV) and/or its systolic dysfunction which is characterized by decreased ejection fraction (EF). In particular, a less 55% ejection fraction (EF) is the cut-off point

10 for LV dysfunction (Wang TJ, Levy D, Benjamin EJ, Vasan RS. The Epidemiology of "Asymptomatic" left ventricular systolic dysfunction: Implications for screening. Ann Intern Med 2003; 138:907-913).

Regardless of its etiology, asymptomatic left ventricular systolic dysfunction (ALVSD) is considered an independent clinical entity as long as it is asymptomatic.

15 Because of its progressive nature, when the ejection fraction (EF) declines below the 40% level, clinical signs, particularly of CHF, enable diagnosis and therapy. Hence it is the covert phase of 55%>EF>40% which remains undiagnosed, and which is prone to deteriorate either into an advanced stage of CHF, or to sudden cardiac death. On the one hand, CHF is considered one of the greatest medical economic burdens in the Western

20 world, and early detection with the appropriate relative medical therapy would significantly improve the outlook of these patients. On the other hand, the largest population of patients with the ALVSD condition consists of individuals who have unrecognized coronary heart disease (CHD), including hibernating myocardium. The annual mortality, for example, of fatal arrhythmias in untreated hibernating myocardium

25 is 16% (Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. "Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery

- 2 -

disease and left ventricular dysfunction: a meta-analysis.", J Am Coll Cardiol 2002; 39:1151-1158).

      As the incidence of ALVSD in the community ranges from 3-7.7% (Wang TJ, Evans JC, Benjamin EJ, Levy D, LeRoy EC, Vasan RS., "Natural history of
5 asymptomatic left-ventricular systolic dysfunction in the community", Circulation 2003; 108:977-982), the only effective way to reduce the risks of ALVSD would be by diagnostic screening of the community (Wang TJ, Levy D, Benjamin EJ, Vasan RS., "The Epidemiology of "Asymptomatic" left ventricular systolic dysfunction: Implications for screening", Ann Intern Med 2003; 138:907-913).

10   Techniques for non-invasive measuring and monitoring various hemodynamic parameters of a patient, such as cardiac parameters, utilizing body bioimpedance techniques have been developed. Some of such techniques are disclosed for example in the following patent publications: WO 02/078539, WO 97/24984, US 5,469,859, US 5,735,284, all assigned to the assignee of the present application.

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SUMMARY OF THE INVENTION

      There is a need in the art to facilitate early diagnostics of the left-ventricular (LV) dysfunction. The technologies available for diagnosing LV dysfunction (EF<55%), like echo-cardiography, radionuclide ventriculography, and cardiac
20 catheterization, are too expensive, and therefore impractical for screening ALVD.

      The present invention provides a novel technique for simple and precise monitoring of the patient's condition enabling early diagnostics of the LV dysfunction. The invented technique utilizes bioimpedance measurements, namely measurement of a basic signal $\Delta R/R$ (or $\Delta Z/Z$) where ΔR or ΔZ is the peripherally depicted signal which is
25 a reliable signal in representing the original source of the pure resistance change or impedance change, and multiplies the $\Delta R/R$ or $\Delta Z/Zo$ parameter by a systolic peak time parameter (α)

      The inventors have found that a product of a first data, indicative of the patient's heart rate, and a second data, indicative of bioimpedance variations during the systolic
30 peak time of the patient's cardiac cycle, can be related to a certain predetermined value,

- 3 -

and this relation is indicative of the left ventricular function. The predetermined value, discovered by the inventors and termed *"Granov-Goor index"* or *"GGI"*, appears to be a threshold defining a boundary between the healthy and diseased conditions with respect to the left ventricular function.

5   In some embodiments of the invention, the first data indicative of the patient's heart rate comprises a patient's heart rate value. Preferably, however, this first data indicative of the patient's heart rate comprises a product of the patient's heart rate value and a certain coefficient k_{HR}. The latter is specific for a patient, and presents a correction coefficient for correction of α, which is the systolic peak time of a cardiac cycle. This

10 correction coefficient k_{HR} is determined as follows:

   it is equal to 1 when the measured patient's heart rate HR_{meas} is within a certain range of normal values between a bottom limit BL and a top limit TL (which range is 60-90 according to the existing standards);

   it is equal to BL/HR_{meas} when the measured patient's heart rate HR_{meas} is less

15 than the bottom limit BL of the normal range; and

   it is equal to TL/HR_{meas} when the heart rate HR_{meas} is higher than the top limit TL of the normal range.

   As for the second data, indicative of electrical bioimpedance changes during the systolic peak time of cardiac cycle, it in some embodiments of the invention is defined

20 as a product of a normalized systolic impedance variation, $\Delta R/R$, and the systolic peak time.

   Thus, considering the first data to be $(HR_{meas} \cdot k_{HR})$ and the second data to be $(\frac{\Delta R}{R} \cdot \alpha)$, the certain predetermined value, being a threshold defining a boundary between the healthy and diseased conditions with respect to the left ventricular function,

25 is equal to 10. In other words, a relation $\frac{\Delta R}{R} \cdot \alpha \cdot HR \cdot k_{HR} < 10$ corresponds to a condition of the left-ventricular dysfunction, and a relation $\frac{\Delta R}{R} \cdot \alpha \cdot HR \cdot k_{HR} \geq 10$ corresponds to a healthy condition with this respect. It should be noted that, in order to provide well correlation of the measurement technique of the present invention with the

- 4 -

common function assessment tools, the range of measured values for $\frac{\Delta R}{R} \cdot \alpha \cdot HR \cdot k_{HR}$ is limited to a certain number, let's say 12, beyond which there is no diagnostic meaning.

Thus, according to one broad aspect of the invention, there is provided a method for determining a patient's heart condition, the method comprising:

5   -   providing first data indicative of the patient's heart rate;

       -    providing second data indicative of bioimpedance peak value during a cardiac cycle;

       -    determining a relation between a product of said first and said second data and a certain predetermined value, said relation being indicative of the patient's left

10   ventricular condition enabling to identify left ventricular dysfunction.

According to another broad aspect of the invention, there is provided a system for use in determining a patient's heart condition, the system comprising:

a data input utility for receiving first data indicative of the patient's heart rate and receiving second data indicative of bioimpedance peak value during a cardiac cycle;

15   a data processing and analyzing utility configured for determining a product of said first and said second data, determining a relation between said product and a certain predetermined value, and based on said relation generating data indicative of the patient's left ventricular condition; and

a data output utility for exposing to user data indicative of the patient's left

20   ventricular condition.

The data input utility may be responsive to user entered data comprising at least one of said first and second data, and/or responsive to output data of a measurement device comprising at least one of said first and second data. In the latter case, the data input utility comprises an appropriate communication unit for connecting to

25   measurement device(s), via wires or wireless signal transmission.

The above-described system is typically a computer system, which may include any other hardware/software, such as memory, data presentation (e.g. display), etc.

The data processing and analyzing utility is configured and operable (programmed) to receive the first and second input data and process them to determine

30   whether the product of said first and said second data satisfies a predetermined condition (namely whether the product of said first and said second data is less than said

- 5 -

certain predetermined value) and, if so, generating data indicative of whether the condition of the patient's left ventricular dysfunction exists or not. It should be understood that the data processing and analyzing utility may calculate the first and second data based on, respectively, the input measured heart rate, and the measured

5   values of $\Delta R/R$ or $\Delta Z/Z_0$ and α.

BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be carried out in practice, embodiments will now be described, by way of non-limiting example only,

10   with reference to the accompanying drawings, in which:

Fig. 1 is a schematic illustration of a system according to the invention for use in determining a patient's heart condition;

Fig. 2 is a flow chart of an example of a method according to the invention for use in determining a patient's heart condition; and

15   **Fig. 3** illustrates the bioimpedance peak systolic value and α during a cardiac cycle.

DETAILED DESCRIPTION OF EMBODIMENTS

Referring to **Fig. 1**, there is illustrated, by way of a block diagram, a monitoring

20   system **10** according to the invention. The system **10** is configured and operable for determining a patient's heart condition. The system **10** is typically a computer system including *inter alia* a data input utility **10A**, a data processing and analyzing utility **10B**, a data output utility **10C** (e.g. display).

The data input utility is configured for receiving data indicative of the patient's

25   heart rate (constituting first data) and for receiving data indicative of bioimpedance variations during a cardiac cycle (constituting second data). The data input utility may include keyboard or the like for entering user data, and/or may include an appropriate communication utility (not shown) for connecting (via wires or wireless) to external measurement device(s) **12**, and/or for connecting to external database. In the present

30   specific but not limiting example, the system connection to two measurement devices

- 6 -

12A and 12B is shown, for receiving the first and second data respectively. In the present example, the first input data piece includes the patient's heart rate value, and the second input data piece includes data indicative of bioimpedance variations during a cardiac cycle. Such bioimpedance variations during a cardiac cycle are illustrated in

5   Fig. 3, showing the bioimpedance change ΔR relative to the base value R during the cardiac cycle. The cardiac cycle includes an ejection time ET interval and the remaining diastola. It should be understood that the second data coming from the measurement device actually includes results of one or more measurement sessions, each including more than one cardiac cycle.

10   The data processing and analyzing utility 10B is preprogrammed for calculating a product of the first and said second data, and determining a relation between this product and a certain predetermined value. The determined relation is indicative of the patient's left ventricular condition. The processing results are then exposed (e.g. displayed) to user. More specifically, the data processing and analyzing utility operates

15   to determine whether said product of the first and said second data is less than said certain predetermined value, and if so generating data indicative of the condition of the patient's left ventricular dysfunction.

In some embodiments of the invention, the data processing and analyzing utility receives the measured heart rate value and defines a correction coefficient k_{HR} as

20   follows:

$k_{HR}=1$ if HR_{meas} is within a certain range of normal values between a bottom limit BL (e.g. 60) and a top limit TL (e.g. 90);

$k_{HR}=BL/HR_{meas}$ when $HR_{meas}<BL$, and

$k_{HR}=TL/HR_{meas}$ when $HR_{meas}>TL$.

25   Then, the first data is determined as $(HR \cdot k_{HR})$.

Independently, the data processor and analyzing utility operates to receive the respective measured data and determine the second data as a product $(\Delta R/R \cdot \alpha)$.

Then, the data processing and analyzing utility operates to determine a product between the first and second data, $(HR \cdot k_{HR} \cdot \Delta R/R \cdot \alpha)$.

30   Thereafter, the above product is analyzed with respect to a predetermined threshold value, which as found by the inventors is being equal to 10.

- 7 -

The physical meaning of the product (HR · k_{HR} · AR/R · α) is associated with the following: As can be understood from the illustration in **Fig. 3**, the value (1/2(HR · k_{HR} · AR/R · α)) actually characterizes the blood volume ejected during the peak systolic time of the cardiac cycle, thus characterizing the condition of the left ventricular activity of

5   the patient, because the left ventricular operation is dominant during the peak systolic time of the cardiac cycle.

Reference is made to **Fig. 2** exemplifying a method according to the invention for determining the patient's left ventricular condition. As shown, the heart rate data (first data) and bioimpedance systolic peak value (SPV) during the cardiac cycle

10 (second data) are independently provided (step 100) and (step 102). These data pieces are processed to calculate the product thereof and determine a relation between this product and a certain threshold value (TV), e.g. 10 (step 104). If the product value is less than TV, then the patient's heart condition is considered as having left ventricular dysfunction (step 106) and if the product is higher or equal to said TV, then the

15 condition is considered as being normal (healthy) – step 108. As indicated above, the

diagnostic meaning of the measured values for $\dfrac{AR}{R} \cdot \alpha \cdot HR \cdot k_{HR}$ larger than the certain

value (e.g. 12) is treated by a physician as those equal to 12.

The following are the experimental results for 60 patients. Table 1 below illustrates the measurement and calculation results for such parameters as heart rate

20 (HR), cardiac index (CI), and Granov-Goor Index (GGI) and Ejection Factor (EF) which characterize the left ventricular condition according to different models. The GGI model is described above, namely is based on a relation between GGI and the product (HR · k_{HR} · AR/R · α); and the EF model is the conventional one based on the interpretation of echo measurements. In this connection, it should be noted that the

25 results of the EF model are relatively subjective as being highly dependent on the physician's interpretation of the measurement results, while the GGF model provides a clear and objective result. The heart rate can be obtained from the ECG measurement or from the impedance wave. As for the cardiac index CI it can be derived from the measured cardiac output AR/R as CI=(AR/R)/BSA, where BSA is the body surface area.

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- 8 -

Table 1:

Patient No	Sex	Age	CI lit/min/m²	GGI	HR	EF%
1	F	57	3.5	11	75	55
2	M	59	3.1	11	76	60
3	M	44	6	18	89	71
4	M	54	4.3	15	75	66
5	M	45	4.2	14	69	60
6	F	50	2.7	11	52	60
7	M	55	3.4	10	81	60
8	M	78	3	9.1	80	50
9	M	71	3.4	12	59	70
10	F	72	2.6	8.3	66	37
11	F	53	2.3	7.9	61	55*
12	F	64	2.9	16	62	50
13	M	61	2.3	6.1	57	40
14	M	61	3.1	11	60	55
15	M	71	2.4	10	53	60
16	F	65	3.4	11	70	55
17	F	58	4.5	13	62	70
18	M	49	2.9	10	56	50
19	M	67	3.2	13	55	55
20	M	46	3.1	10	62	55
21	M	60	2.4	7.2	66	38
22	M	57	3.9	12	74	63
23	F	57	4.5	14	66	74
24	F	62	3	10	67	58
25	M	64	3.6	12	63	63
26	M	59	3.7	13	70	63
27	F	64	2.4	7.4	74	36
28	F	70	2.6	9.8	59	53
29	F	71	3.3	12	90	57
30	M	74	3.7	12	86	58
31	M	54	2.3	4.3	112	20
32	F	46	3.6	14	70	55
33	M	43	5.1	14	89	55
34	M	47	3.8	12	67	57
35	M	53	3.6	15	55	55
36	M	66	2.4	8.4	50	36
37	M	43	4.1	12	78	60
38	M	48	3.8	12	79	55
39	F	51	3.4	10	76	65
40	F	62	4.1	14	76	56
41	F	51	4.5	15	70	60
42	M	72	4.3	12.7	86	55

43	M	47	3	10.6	58	55
44	F	51	3.6	11.9	60	60
45	F	65	3.4	10.2	67	60
46	F	82	4.2	12.2	76	65
47	M	50	4.3	14.9	67	56
48	M	81	3.1	11.4	63	55
49	M	58	2.4	7.6	61	50
50	M	49	4.4	13.4	88	60
51	M	76	2.4	8	63	50
52	M	54	3.1	9.6	75	53
53	M	55	3.4	11.4	61	60
54	M	62	5.8	14.9	93	65
55	M	48	6.1	16.9	86	60
56	M	60	3.4	11.1	69	56
57	F	76	3.1	12.1	59	60
58	M	58	3.4	13.5	55	59
59	M	53	3.6	11.1	79	57
60	M	45	4.8	12.8	89	56

As can be seen from the above experimental results, the invented GGI model provides for better sensitivity, specificity, and positive and negative predictive values, as compared to the EF model. This is summarized in Table 2 below.

Table 2:

	Granov-Goor Index	Cardiac Index
Sensitivity	92.31%	61.54%
Specificity	100.00%	97.87%
Positive Predictive Value	100.00%	88.89%
Negative Predictive Value	97.92%	90.20%

- 10 -

CLAIMS:

      1.   A method for use in determining a patient's heart condition, the method comprising:

- providing first data indicative of the patient's heart rate;

5   - providing second data indicative of bioimpedance peak value during a cardiac cycle;

- determining a relation between a product of said first and said second data and a certain predetermined value, said relation being indicative of the patient's left ventricular condition enabling to identify left ventricular dysfunction.

10   2.   A method according to Claim 1, wherein said relation indicative of the patient's left ventricular dysfunction is determined such that said product of said first and said second data being less than said certain predetermined value corresponds to a condition of the patient's left ventricular dysfunction.

      3.   A method according to Claim 1, wherein said first data indicative of the 15 patient's heart rate comprises a patient's heart rate value.

      4.   A method according to Claim 1, wherein said first data indicative of the patient's heart rate comprises a product of the patient's heart rate value and a coefficient k_{HR} which is specific for a patient and which is a correction coefficient for correction of the heart rate.

20   5.   A method according to Claim 4, wherein the correction coefficient k_{HR} is equal to 1 when the measured patient's heart rate HR_{meas} is within a certain range of normal values between a bottom limit BL and a top limit TL, is equal to BL/HR_{meas} when the measured patient's heart rate HR_{meas} is less than the bottom limit BL of the normal range, and is equal to TL/HR_{meas} when the heart rate HR_{meas} is higher than the 25 top limit TL of the normal range.

      6.   A method according to Claim 5, wherein the correction coefficient k_{HR} is equal to 1 when the measured patient's heart rate HR_{meas} is within a range of 60-90, and is equal to $60/HR_{meas}$ when the measured heart rate HR_{meas} is less than 60, and is equal to $90/HR_{meas}$ when the measured heart rate HR_{meas} is higher than 90.

30   7.   A method according to Claim 1, wherein said second data indicative of electrical bioimpedance changes during a cardiac cycle comprises a product of a normalized systolic impedance variation, $ΔR/R$, and a systolic peak time, $α$.

8.   A method according to Claim 5, wherein said second data indicative of electrical bioimpedance changes during a cardiac cycle comprises a product of a normalized systolic impedance variation, $\Delta R/R$, and a systolic peak time, α.

9.   A method according to Claim 6, wherein said second data indicative of electrical bioimpedance changes during a cardiac cycle comprises a product of a normalized systolic peak value impedance, $\Delta R/R$, and a systolic peak time, α.

10.   A method according to Claim 9, wherein said certain predetermined value is equal to 10.

11.   A system for use in determining a patient's heart condition, the system comprising:

        a data input utility for receiving first data indicative of the patient's heart rate and receiving second data indicative of bioimpedance variations during a cardiac cycle;

        a data processing and analyzing utility configured for determining a product of said first and said second data, determining a relation between said product and a certain predetermined value, and based on said relation generating data indicative of the patient's left ventricular condition; and

        a data output utility for exposing to user data indicative of the patient's left ventricular condition.

12.   A system according to Claim 11, wherein said data input utility is responsive to user entered data comprising at least one of said first and second data.

13.   A system according to Claim 11, wherein said data input utility is responsive to output data of a measurement device, said output data comprising at least one of said first and second data.

14.   A system according to Claim 12, wherein said data input utility is responsive to output data of a measurement device, said output data comprising at least one of said first and second data.

15.   A system according to Claim 11, wherein said data processing and analyzing utility operates to determine whether said product of said first and said second data is less than said certain predetermined value and generating data indicative the condition of the patient's left ventricular dysfunction.

16.   A system according to Claim 11, wherein said first data indicative of the patient's heart rate comprises a patient's heart rate value.

- 12 -

17.   A system according to Claim 11, wherein said first data indicative of the patient's heart rate comprises a product of the patient's heart rate value and a coefficient k_{HR} which is specific for a patient and which is a correction coefficient for correction of the heart rate.

18.   A system according to Claim 17, wherein the correction coefficient k_{HR} is equal to 1 when the measured patient's heart rate HR_{meas} is within a certain range of normal values between a bottom limit BL and a top limit TL, is equal to BL/HR_{meas} when the measured patient's heart rate HR_{meas} is less than the bottom limit BL of the normal range, and is equal to TL/HR_{meas} when the heart rate HR_{meas} is higher than the top limit TL of the normal range.

19.   A system according to Claim 18, wherein the correction coefficient k_{HR} is equal to 1 when the measured patient's heart rate HR_{meas} is within a range of 60-90, and is equal to $60/HR_{meas}$ when the measured heart rate HR_{meas} is less than 60, and is equal to $90/HR_{meas}$ when the measured heart rate HR_{meas} is higher than 90.

20.   A system according to Claim 11, wherein said second data indicative of electrical bioimpedance changes during a cardiac cycle comprises a product of a normalized systolic impedance variation, $\Delta R/R$, and a systolic peak time, α.

21.   A system according to Claim 18, wherein said second data indicative of electrical bioimpedance changes during a cardiac cyclecomprises a product of a normalized systolic impedance variation, $\Delta R/R$, and a systolic peak time, α.

22.   A system according to Claim 19, wherein said second data indicative of electrical bioimpedance changes during a cardiac cycle comprises a product of a normalized impedance variation, $\Delta R/R$, and a systolic peak time, α.

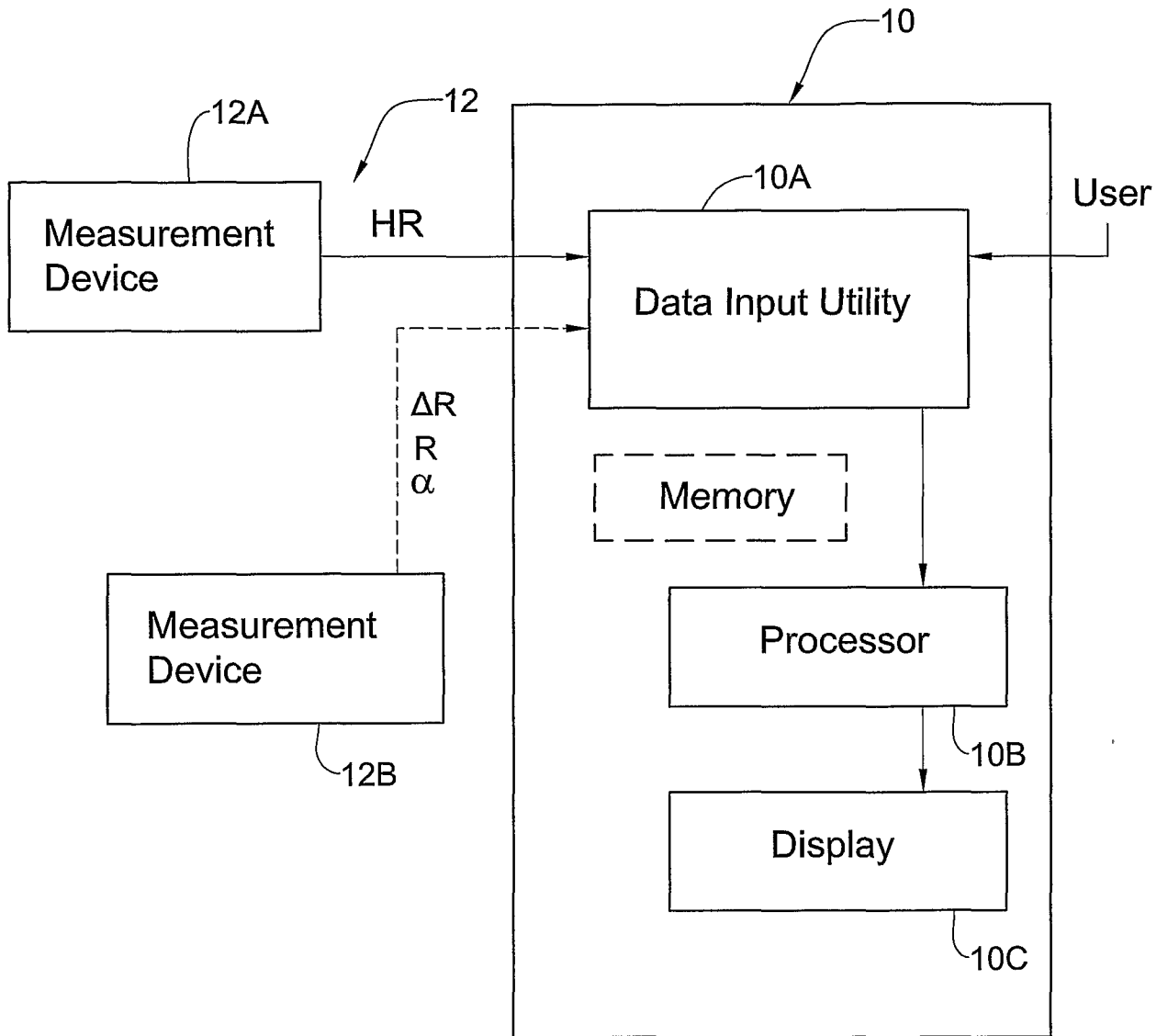23.   A system according to Claim 21, wherein said certain predetermined value is equal to 10.
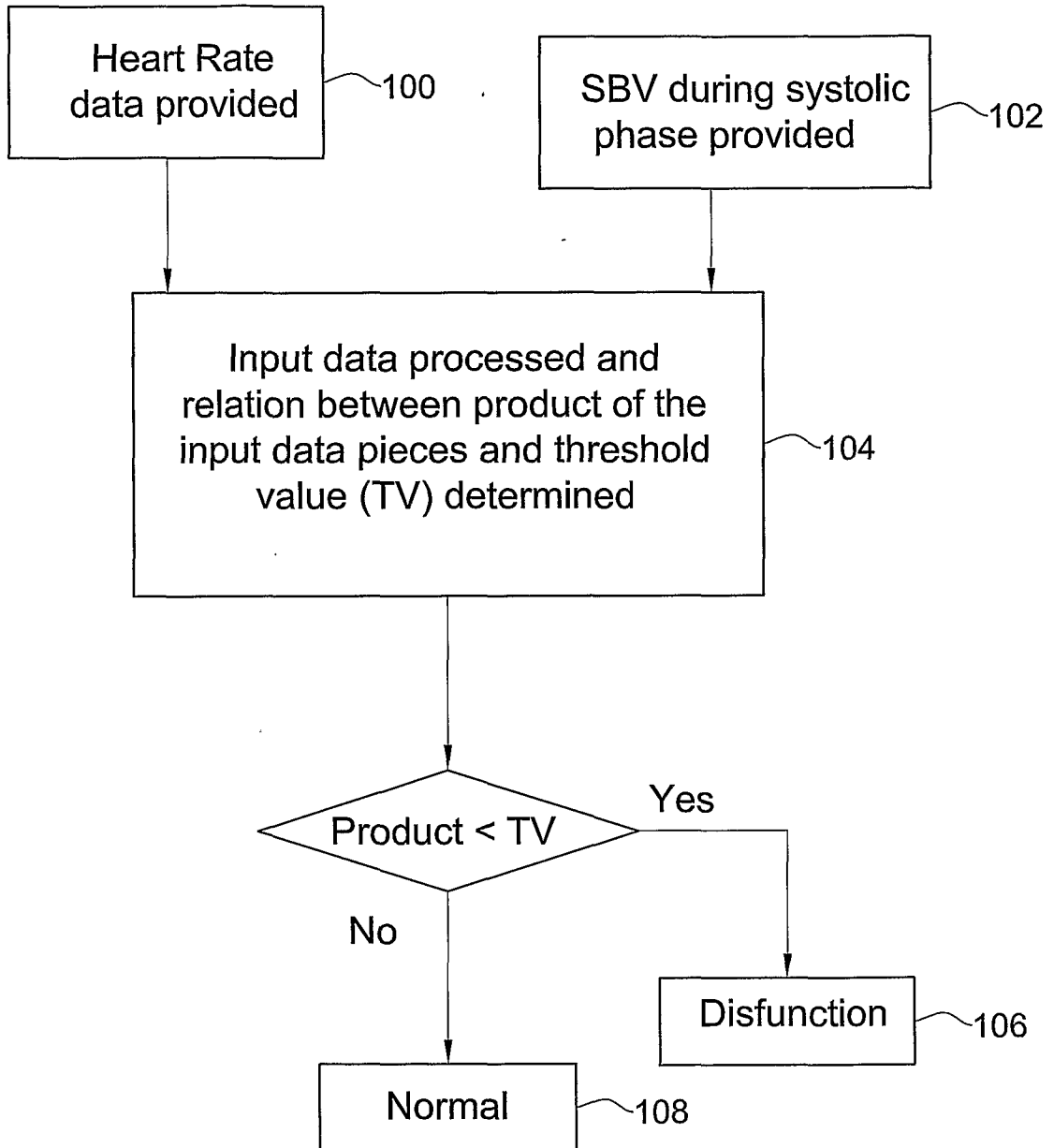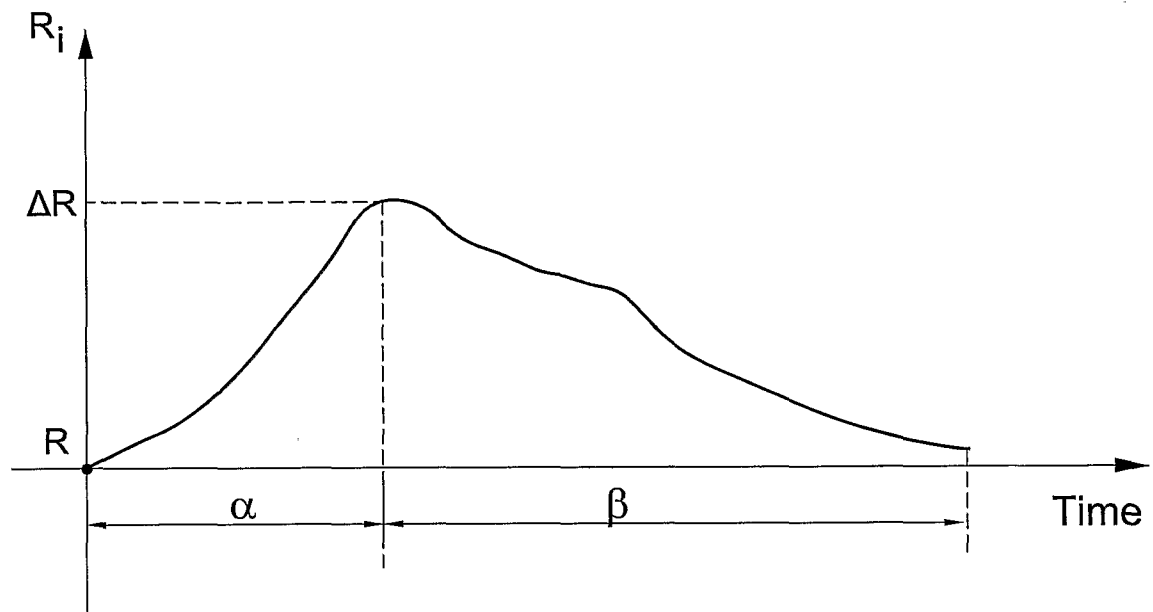
1/3

FIG. 1

FIG. 2

FIG. 3