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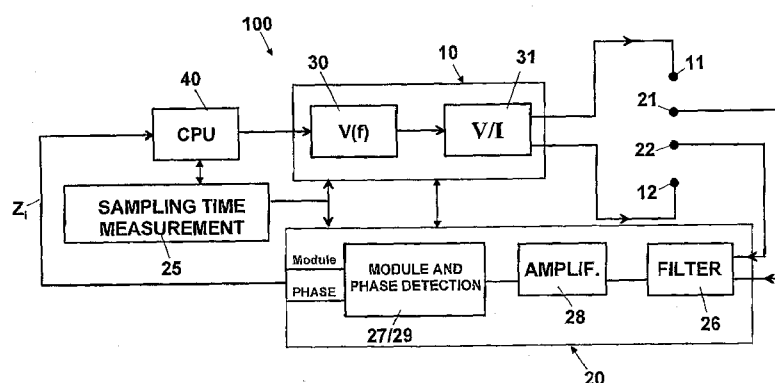
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(54) Title: A WEARABLE DEVICE FOR EARLY DIAGNOSIS OF CARDIOPATHY AND/OR CARDIOVASCULAR DISEASES WHICH CAN BE DETERMINED BY HEMODYNAMIC VARIABLES

Fig. 1

(57) Abstract: A early diagnosis device (100) of cardiopathies in a patient (50) such as a cardiac decompensation and/or cardiovascular diseases comprises a wearable support (1) and a diagnostic unit (5) mounted to the wearable support (1). The diagnostic unit (5) comprises a means for delivering (10) an electric current stimulus (I_i) at a predetermined frequency (f_i) to the patient's body (50) and a means for measuring (20) a thoracic electrical bioimpedance (Z_i), which is adapted to provide a bioelectric impedance signal (Z_i) on the basis of the electric stimulus (I_i) at the predetermined frequency (f_i). The device (100) further comprises an adjustment means (30) for adjusting the frequency (f_i) of the electric stimulus (I_i) in way suitable for transmitting a plurality of electric stimuli ($I_1, I_2, \dots, I_n$) at respective different frequencies ($f_1, f_2, f_3, \dots, f_n$) and such that the means for measuring (20) detects a corresponding complex bioimpedance signal ($Z_1, Z_2, Z_3, \dots, Z_n$). In addition, the device comprises a memory (35) that is configured to store the complex bioimpedance signals at a first time (t_1), at a second time (t_2) and at an nth time (t_n) and a means for extracting the real part ($R_1, R_2, R_3, \dots, R_n$) of the complex signals for instants (t_1, t_2, t_n), to obtain a respective time chart (C_1, C_2, C_n) of the real part for each frequency. Furthermore, it comprises a means for analysing (40) the time chart (C_1, C_2, C_n) and a means to provide an alarm (46) of cardiac decompensation if a decrease value DR/Dt is higher than a predetermined value DR_0/Dt .

TITLE

A WEARABLE DEVICE FOR EARLY DIAGNOSIS OF CARDIOPATHY AND/OR
CARDIOVASCULAR DISEASES WHICH CAN BE DETERMINED BY
HEMODYNAMIC VARIABLES

DESCRIPTIONScope of the invention

The present invention relates to medical devices and, in particular, it relates to a wearable device for cardiopathy or cardiovascular diagnosis in a patient and/or for detecting hemodynamic variables. In particular, the device is used for diagnosis of cardiopathies, for example cardiac decompensation, or for measuring hemodynamic useful for diagnosis of such pathologies.

Description of the technical problem

As well known, cardiovascular diseases, in particular cardiopathies such as cardiac decompensation, can be correlated to accumulation of fluids/liquids in the body, to their flow and to their variation with time.

The prevention and the early diagnosis of such cardiopathies is carried out by detecting any serious hydro-electrolytic alterations that can cause the diseases such as, for example, anasarca, declive edema, acute pulmonary edema etc.

On the other hand, it is known that through bioimpedance techniques it is possible to measure the presence of liquids in the human body and their variation with time. In particular, known devices for measuring the bioimpedance provide injecting through the skin in a subject an alternated current at a fixed frequency of 50-70 kHz, by two surface electrodes called injectors. A second couple of electrodes, called sensors, has instead the task of

measuring the subsequent voltage, which follows the opposition by the body to the current at fixed frequency applied by the above described injection electrodes.

This opposition to the current is called Impedance Z and is based on the principle that the current follows a path of minimum electric resistance. Such value of impedance Z can be represented by a complex number, and therefore formed by a real and an imaginary part, or also by a module and by a phase. More precisely, the current flows through the fluids, in particular water, and, the opposition to the current can be correlated (inversely proportional) to the volume of water in the body. In other words, a higher amount of liquid determines a lower value of the bioimpedance module and vice-versa.

As well known, in subjects involved with cardiac decompensation, the value of the bioimpedance module monitored in previous days to the occurrence of the symptoms is decreasing progressively up to reaching a minimum value where the disease becomes symptomatic.

The known devices for measuring the bioimpedance inject the current at a single frequency, and are not for this reason adapted to provide a reliable monitoring. In particular, the variation of the bioimpedance determined at a single frequency is not strictly correlable to the variation of the fluids caused by a worsening of the cardiac function, because it can be also correlated to other parameters of the patient same. In fact, by at least one bioimpedance measurement at fixed frequency, it is not possible to discriminate precisely between intra or extra cellular liquids. It is therefore difficult to determine the causes of the variation of the impedance, both of its module and of its phase. Such alteration and its amount, for example, can be generated by a variation of the fat

mass of the patient and influenced by other physical factors such as sex, weight, age or even daily habits.

In addition to what above defined, the known devices based on the bioimpedance measurement are not adapted to obtain a functional monitoring of the patient for a long time. In fact, among the known bioimpedance measurement devices there are bulky and expensive ones. For this reason, often, such diagnosis has to be limited to hospitals or nursing homes, causing a long monitoring to be problematic, which would be instead much easier with laptop devices.

On the other hand, the use of laptops, which would be possible by application of bioimpedance measuring instruments mounted to special wearable supports, is presently not much reliable, since the detection can be strongly affected by different factors, such as the different positioning by the patient or nursing operators of the sensors at any successive detections, as well as by movements of the patient, or by changes of patient's skin conditions with respect to the electrodes, etc., and therefore the measurements obtained would be not easily correlable to each other, in order to determine a helpful clinical picture that can reveal and prevent the onset of a cardiopathy.

In other words, the known bioimpedance measuring systems, in particular those that can determine the onset of cardiopathies, can be problematic and do not allow to obtain reliable values of changes of the body fluids, especially in a wireless monitoring scenario. For this reason, values observed by such measuring devices should be always associated and backed by other types of detection and analysis devices.

A further analysis for diagnosis of cardiovascular diseases is the impedance cardiography (Impedance Cardiography, ICG), also-called thoracic bioimpedenziometry or impedance pletismography, and, in particular, it relates
5 to the study of the cardiac functionality by measuring the electric impedance of the thorax.

It is a non invasive technique capable of providing data on important hemodynamic parameters and on the thoracic content of liquid. The variation of impedance, determined
10 through electrodes applied to the thorax, is generated by fluctuations in the volume of blood and in the blood speed, mainly with respect to the rising aorta tract, during the cardiac cycle.

The known ICG devices provide monitoring the patient in a
15 hospital to measure the thoracic impedance from which different hemodynamic variables can be measured in a predetermined moment of a day. For long monitoring periods, the patient must every day make a measurement, in order to obtain, after a plurality of measurements, a clinic picture
20 enough complete for a diagnosis of the cardiac diseases.

On the other hand the use of wearable ICG devices to long daily monitoring for more days are very unreliable. In fact, also in this case the measure can be strongly affected by factors such as the arrangement of the
25 electrodes, the movement of the patient, the variation of the interface conditions of the skin with the electrodes, etc.

In WO2004/030535 a method is described for measuring the volume, the composition and the movement (HZV) of electro-
30 conductive body fluids, based on the Impedance Cardiography (ICG) for determining hemodynamic parameters.

In US 2006/184060 an implantable device is described that comprises electrodes implantable in the patient's body

capable of making current signals at different frequencies in order to calculate impedance values. In this case, the implanted electrodes are not subject to problems of variability owing to the interface with the skin of the user, but it is an invasive device.

In MART MIN ET AL: "Synchronous Sampling and Demodulation in an Instrument for Multifrequency Bioimpedance Measurement" a multichannel system is described for non-invasive diagnosis of cardiovascular diseases associated with Impedance CardioGraphy (ICG).

Summary of the invention

It is therefore a feature of the present invention to provide a wearable device for diagnosis of the cardiac decompensation and/or for detecting hemodynamic variables in a patient, which allows a precise and reliable detection.

It is also a feature of the present invention to provide a wearable device for diagnosis of the cardiac decompensation and/or for detecting hemodynamic variables in a patient that is modular and reconfigurable in its aspect and components.

It is a further feature of the present invention to provide a wearable device for diagnosis of the cardiac decompensation and/or for detecting hemodynamic variables in a patient where the only sensing components of the device are developed, in order to be minimally invasive for the patient and capable of interfacing in a comfortable way for the user, with easy and univocal connections.

It is also a feature of the present invention to provide a wearable device for diagnosis of the cardiac decompensation and/or for detecting hemodynamic variables in a patient that allows long lasting monitoring outside of hospitals or nursing homes.

These and other objects are achieved by a device for early diagnosis in a patient for cardiopathies such as a cardiac decompensation and/or cardiovascular diseases which can be determined by detecting hemodynamic variables of the patient said device for diagnosis comprising:

- a wearable support;
- a diagnostic unit mounted to said wearable support, said diagnostic unit comprising:
 - a means for delivering an electric stimulus I_i at a predetermined frequency f_i to the body of said patient,
 - a means for measuring a thoracic electrical bioimpedance Z_i of the body of said patient by providing a bioelectric impedance signal on the basis of said electric stimulus I_i at said predetermined frequency f_i ;
 - an adjustment means for adjusting said frequency of said electric stimulus I_i such that a plurality of electric stimuli is delivered $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, \dots f_n$, said means for measuring the thoracic electrical bioimpedance Z_i configured to measure a corresponding complex bioimpedance signal $Z_1, Z_2, Z_3 \dots Z_n$ for each of said plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, \dots f_n$, and to provide a plurality of complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$;
 - a memory that is configured to store said plurality of complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ at a first time t_1 , at a second time t_2 and at an nth time t_n ;
 - a means for generating a plurality of complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ recorded in

said memory at said first time t_1 , second time t_2 and nth time t_n ,

- a means for extracting the real part $R_1, R_2, R_3 \dots R_n$ of said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ to obtain a respective time chart C_1, C_2, C_n of said real part for each frequency $f_1, f_2, \dots f_n$ at the times $t_{(1)}, t_{(2)}, \dots t_n$;
- a means for analysing said time chart C_1, C_2, C_n of said real part $R_1, R_2, R_3 \dots R_n$, in order to obtain a decrease rate with time of said real part for each frequency $f_1, f_2, \dots f_n$ and to calculate a decrease value DR/Dt ;
- an alarm means to provide an alarm of cardiac decompensation associated with said means for analysing, said alarm generated if said decrease value DR/Dt is higher than a predetermined value DR_0/Dt .

Advantageously, said means for analysing comprises a sampling means that is configured to operate said means for delivering and said means for measuring in a predetermined time range, in order to repeat a plurality of said bioimpedance measurements at times $t_1, t_2, \dots t_n$ that are distant said time range from each other.

Preferably, said sampling time range is one day, and said number n of times $t_1, t_2, \dots t_n$ is set between 7 and 30 days, preferably 14 days.

Advantageously, said means for analysing is configured to compare said time chart of the real part $R_1, R_2, R_3 \dots R_n$ of the complex bioimpedance signals determined on the patient also with characteristic time charts of a cardiopathy by means of clinical data of said patient, in order to increase the amount of data to compare and to obtain a more precise prediction, in particular said

clinical data describing the health status of the patient and being selected from the group consisting of: age, sex, weight, fat-free mass index, etc.

Advantageously, said means to provide an alarm comprises an acoustic emitter.

Preferably, the following are further provided:

- a means for extracting the imaginary part $L_1, L_2, L_3 \dots L_n$ of said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ to obtain a respective time chart of said imaginary part for each frequency $f_1, f_2, \dots f_n$ at the times $t_{(1)}, t_{(2)}, \dots t_n$;
- a means for analysing said time chart of said imaginary part $L_1, L_2, L_3 \dots L_n$, in order to obtain a rate of variation with time of said imaginary part for each frequency $f_1, f_2, \dots f_n$ and to calculate a variation value DL/Dt ;
- a means to provide a cardiac decompensation parameter associated with said means for analysing if said variation value DL/Dt exceeds the limits by a predetermined range.

Advantageously, said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ are calculated as average values within a predetermined measurement range, in particular set between 3 and 10 minutes.

In particular, said means for delivering an electric stimulus is adapted to deliver a current stimulus and comprises:

- a couple of skin injection electrodes at a distance from each other and arranged on the thorax of said patient;
- a variable current frequency generator connected to said skin injection electrodes and associated with said adjustment means that adjust said current

stimulus, such that said adjustment means controls in frequency said current generator such that it injects said plurality of electric stimuli at respective different frequencies, said current having a corresponding predetermined digital numerical series.

Preferably, said different frequencies $f_1, f_2, \dots, f_n$ are comprised in a range set between 1 kHz and a 1MHz and said electric stimuli have an intensity set between 0.1mA and 0.5mA, in particular 0.44mA.

In particular, said means for measuring comprises:

- a couple of skin sensor electrodes arranged substantially between said couple of injection electrodes, said couple of skin sensor electrodes configured to measure a voltage tuned to said plurality of electric stimuli to respective different frequencies;
- a means for transforming said voltage into a digital numerical series;
- a means for calculating the bioimpedance module as ratio between the absolute values of said digital numerical series responsive to said voltage and of said digital numerical series responsive to said current stimulus at a predetermined frequency f_i , in order to obtain a corresponding digital numerical signal of the bioimpedance module;
- a means for calculating the bioimpedance phase as phase shift time between said voltage and said current stimulus at a predetermined frequency f_i , in order to obtain a corresponding signal of the bioimpedance phase;
- a means for converting said signal of the bioimpedance phase into a respective digital numerical signal.

This way, the couple of skin sensor electrodes measure a voltage V_{f1} tuned to the current stimulus I_{f1} at frequency f_1 . By the ratio $V_{f1}/I_{f1}=Z_{f1}$ the module of the bioelectric impedance signal Z_{f1} can be obtained relative to frequency f_1 . By changing the frequency of the current I for a predetermined frequency band the modules of the bioimpedance signals Z_{f1} , Z_{f2} , Z_{f3} , ... Z_{fn} are obtained.

In the same way, for each voltage value V_{fi} tuned to the current stimulus I_{fi} at frequency f_i the delay time Δt_i of the injected current signal I_{fi} is compared with the measured voltage signal V_{fi} .

This way, the analysis of the complex bioimpedance signals, obtained starting from a plurality of electric stimuli at different frequencies, makes it possible to obtain a reliable measurement by computing a plurality of complex bioimpedance signals at different frequencies. A time chart can thus be generated of such complex values, i.e. of the bioimpedance module and phase, comparable with charts/complex patterns typical of the onset of cardiopathies.

In particular, said means for determining the module and the phase of each of said complex bioimpedance signals comprises a amplifier a band-pass filter.

Advantageously, said means for analysing comprises:

- a programmable logic unit that contains said means for analysing;

- a memory connected to said programmable logic unit;

wherein said programmable logic unit is associated with said sampling means, with said means for delivering and with said means for measuring, in order to select a predetermined frequency f_i of said electric stimulus, for generating and analysing said plurality of complex bioimpedance signals, in particular the modulus and

phase signals at said different frequencies $f_1, f_2, \dots, f_n$, in a way to generate said time chart and compare it with a time chart typical of a cardiopathy present in said memory. This way, it is possible to evaluate the evolution with time of said complex bioimpedance signals measured at the different frequencies. It is then possible to recognize and compare the trend obtained for the patient with other trends, determined with the same technique, which describe a time chart feature that resembles the typical onset of cardiopathies.

In other words, the bioimpedance signals obtained with multifrequency measurements of a patient for a period of more days, are computed in order to obtain for each day a characteristic chart that describes the trend of such complex values, for example within one day.

Each daily chart will then added to other data, in order to obtain a set of charts that as a time chart, for example a weekly chart. The chart is compared by a comparison means with further bioimpedance charts that describe a trend typical of the onset of a cardiopathy.

So, if by the comparison there is a correspondence between the two charts, i.e. that with the known trend and that obtained from the measurement on the patient, an early diagnosis on the onset of the cardiopathy can be achieved.

In particular, said means for comparing can compare said trend of the patient with the characteristic trend. In this case, the comparison can be investigated further also on the basis of the clinical data of the patient, for example the fat mass index, age, sex, weight etc., making it possible to obtain a even higher reliability and then a more precise and accurate preliminary diagnosis.

Advantageously, said means for analysing is further configured to extract from the complex bioimpedance signal,

cardiovascular hemodynamic functionality signals like the cardiac output (volume-minute), the cardiac index, the stroke volume, the system vascular resistance, the flow acceleration index, the flow velocity index, the thoracic fluid content, the cardiac work, the pre-ejection time and ventricular ejection time etc.

In particular, said hemodynamic signals are obtained from a sampling at high frequency, for example 200 samples per second for a predetermined time. In particular, the means for analysing comprises a plurality of known algorithms for analysing the bioelectric impedance signal and to turn it into one of the above cited hemodynamic signals.

In other words, the algorithms applicable to the bioimpedance module and phase signals, taken at different frequencies, are configured to determine the set of the above described hemodynamic variables for each signal at different frequencies. By the comparison and by the control of the values of the hemodynamic variables measured on the signals at the different frequencies, is possible to determine the hemodynamic parameters of the patient in a way reliable and supported by numerical verification. In substance, from the redundancy of the data an increased reliability is achieved. The obtained data can discriminate possible artifacts due to the fact that the device is wearable and used directly by the end user. For example, if some hemodynamic variables obtained to determine frequencies have values higher or less than determined thresholds, the system can communicate for example an positioning error of the electrodes by an alarm.

In particular, said means for analysing is configured to compare said cardiovascular hemodynamic functionality signals with said time chart to obtain a more reliable prediction of said cardiopathy.

Preferably, said couple of injection electrodes and said couple of sensor electrodes are substantially arranged in line, in particular they can be associated with a belt or other wearable element. This way, the relative position of the electrodes remains fixed, in order to reduce the artifacts of the measure due to a wrong or inaccurate positioning.

In particular, said device further comprises an interface means that is configured to transfer the collected and computed data to a central collection and correlation unit which can correlate it with other signals.

Preferably, said interface means is a wireless or wired interface means.

Alternatively, said interface means comprises a coupling means that is arranged to provide a matching shape with said central collection unit. In case of a wireless interface or an interface with matching shape the wearable device can monitor the patient for a long period, for example 24h. For example, the patient can wear the device during a whole day during which more bioimpedance signals are determined and recorded for eventually generating a time chart, for example in a several days time. Such chart, can then be compared with a known trend of known bioimpedance values in case of a cardiopathy, which allows an early diagnosis thereof and then permits to adopt preventive measures.

Advantageously, said interface means can be used for combining the device with other sensor devices and modules, such as an accelerometer, an electrocardiograph, a device for pulse oximetry that measures the concentration of oxygen in the blood, a module for measuring the pressure, the temperature etc.

Brief description of the drawings

The invention will be now shown with the following description of an exemplary embodiment thereof, exemplifying but not limitative, with reference to the attached drawings in which:

- 5 - Fig. 1 shows a diagrammatical view of a wearable device for early diagnosis of cardiopathies, according to the invention;
- Fig. 2 shows a diagrammatical view of the wearable device of Fig. 1 mounted to the thorax of a patient;
- 10 - Fig. 3 shows a block diagram that diagrammatically shows the steps of measuring the bioimpedance phase versus the current frequency;
- Fig. 3A shows in particular the step of control and comparison of the data of bioimpedance, in order to
15 obtain a time chart of such values for deriving an early diagnosis on the onset of cardiac diseases, such as a cardiac decompensation;
- Figs. 4 and 5 show a trend of the data of variable frequency bioimpedance obtained from the measurements
20 made by the device of Fig. 1;
- Fig. 6 shows a diagrammatical view of the control of each complex signal of bioimpedance, in order to obtain the chart of Figs. 4 and 5;
- Fig. 7 shows a further application of the device of
25 Fig. 1 that is configured to extract hemodynamic parameters of the patient from the complex bioimpedance signals;
- Fig. 8 shows a perspective view of the device according to the invention mounted to a belt wearable by a
30 patient.

Description of a preferred exemplary embodiment

With reference to Figs. 1 and 2, a diagrammatical view is shown a device 100 of early diagnosis of

cardiopathies in a patient 50 (Fig.2), such as a cardiac decompensation and/or cardiovascular diseases which can be determined by detecting hemodynamic variables. In particular, the patient 50 has determined clinical data
5 that describe the health status, which are then combined with the measurements obtained from the device 100, as described below.

In particular, as diagrammatically shown in Fig. 2, the diagnostic device 100 comprises a wearable support 1 on which a diagnostic unit 5 is arranged that comprises a
10 means for delivering 10 an electric stimulus, in particular a electric current stimulus I_i , at a predetermined frequency f_i , to the patient's body 50, at the thorax 55. Furthermore, the diagnostic unit 5 comprises a means for
15 measuring 20 a thoracic electrical bioimpedance Z_i applied always on the patient's body for providing a bioelectric impedance signal Z_i on the basis of the electric stimulus I_i at a predetermined frequency f_i .

The diagnostic device 100 also comprises, as also
20 shown in Fig. 3, an adjustment means 30 for adjusting the frequency f_i of the electric stimulus I_i , included in the means for generating 10, such that a plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ can be imparted at respective different frequencies $f_1, f_2, f_3 \dots f_n$, such that the means
25 20 for measuring the thoracic electrical bioimpedance detects a corresponding complex bioimpedance signal Z_1, Z_2, Z_3, Z_n for each plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, f_3 \dots f_n$. By the latter it is possible to obtain a plurality of complex
30 bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$.

Furthermore, the device for early diagnosis comprises a memory 35 that is configured to store the plurality of complex bioimpedance signals at a first time t_1 , at a

second time t_2 and at an n th time t_n , and a means for extracting the real part $R_1, R_2, R_3 \dots R_n$ of said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ recorded in said memory 35, respectively at said first time t_1 , second time t_2 and
5 n th time t_n , to obtain a respective time chart C_1, C_2, C_n of said real part for each frequency $f_1, f_2, \dots f_n$ at the times $t_1, t_2, \dots t_n$.

In particular, the sampling time range is one day, and the number n of said times $t_1, t_2, \dots t_n$ is set between 7
10 and 30 days, preferably 14 days.

In addition, the device has a means for analysing 40 the time chart C_1, C_2, C_n (Fig. 4 and 5) of the real part $R_1, R_2, R_3 \dots R_n$, in order to obtain a decrease rate with time of the real part for each frequency $f_1, f_2, \dots f_n$ and to
15 calculate a decrease value DR/Dt .

In addition, device 100 has a means 40 for analysing the time chart of the complex bioimpedance signals Z_1, Z_2, Z_n , in order to obtain a decrease rate with time of the complex signals of impedance Z_1, Z_2, Z_n for each frequency
20 $f_1, f_2, \dots f_n$ and for calculating a decrease value.

Furthermore, associated with the means for analysing 40, a means 46 is provided to provide an alarm of cardiac decompensation, said alarm generated if said decrease value DR/Dt is higher than a predetermined value DR_0/Dt , as
25 described below more in detail.

More in particular, as shown in the block diagram of Fig. 3A, the means for analysing 40 is configured to compare the time chart or data resulting from the real part of the complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$
30 determined on the patient 50, with respect to a trend/data chart of a cardiopathy monitored in a previous time, in order to achieve an early check on the onset of said cardiopathy.

The complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ are calculated as average values within a predetermined measurement range, in particular set between 3 and 10 minutes.

5 In the same way, furthermore, a means can be provided for extracting the imaginary part $L_1, L_2, L_3 \dots L_n$ of the complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ to obtain a respective time chart of said imaginary part for each frequency $f_1, f_2, \dots f_n$ at the times $t_1, t_2, \dots t_n$;

10 The means for analysing (40) compute in this case the time chart of the imaginary part $L_1, L_2, L_3 \dots L_n$, in order to obtain a rate of variation with time of the imaginary part for each frequency $f_1, f_2, \dots f_n$ and to calculate a variation value DL/Dt .

15 For the imaginary part, a means is provided to provide a parameter of cardiac decompensation associated with the means for analysing 40 if the variation value DL/Dt exceeds the limits by a predetermined range.

More in particular, as shown in Fig. 3A, the means for
20 analysing 40 associated with the memory 35 comprises a programmable logic unit 45. The programmable logic unit 45 is associated in turn to the means for delivering 10 and to the means for measuring 20, in order to select a predetermined frequency f_i of the electric stimulus I_{fi} to
25 deliver, and to analyse the corresponding bioimpedance signals Z_{fi} , in particular the signals of module $|Z_i|$ and phase P_i , measured at the different frequencies, in order to compare them with other previous data stored in memory 35. This way, it is possible to evaluate the evolution with
30 time of the real part of the complex bioimpedance signals measured at the different frequencies. It is then possible to recognize and compare the trend obtained for the patient
50 with other trends, determined with the same technique,

which describe a time chart in the many instants t_1, t_2, t_n feature that copy the typical onset of cardiopathies.

This way, the analysis of the real part $R_1, R_2, R_3 \dots R_n$ of the complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ obtained starting from a plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at different frequencies $f_1, f_2, f_3 \dots f_n$, makes it possible to obtain a reliable measurement by computing a plurality of real values of bioimpedance at different frequencies. This way a time chart of such real values can be generated, in particular of the module $|Z|$ and also of the phase P of the bioimpedance, comparable with charts/complex patterns, that are typical in case of onset of cardiopathies, as measured in different times or using characteristic data.

In detail, the use of more currents at different frequencies allows to discard changes of the bioimpedance values that are anomalous and not directly connected to an accumulation of liquid that is characteristic of a potential cardiopathy, but are due to other causes, for example to habits of the patient.

In particular, the charts of the real part of the bioimpedance obtained for each current and frequency, as shown in Fig. 4 and 5, which show a monitoring done in a predetermined period of time, for example 15 days, are computed through a comparison block 55 that has as input the data measured on the patient 50 in different previous instant/daily measurements. Furthermore, also characteristic data can be compared on the basis of the clinical data of patient 50.

Even more in detail, the cardiac decompensation has a low sampling frequency, about a sample per day, i.e. a daily value of bioimpedance daily. To determine this daily value for example a value per second is acquired for a time of 5

min and then the collected data are computed, in order to obtain a single average value, as above described.

The bioimpedance signals obtained on the patient 50 with multifrequency measurements for a period of more days, are computed, in order to obtain characteristic charts as shown in figs. 4 and 5. In particular, Fig. 4 depicts the bioimpedance module, or real part, versus the frequency for days 1, 2.. N. In This way, it is possible to observe the trend of variation of this quantity in more days.

As shown in Fig. 5, it is, furthermore, possible to return the values of module (shown) and phase (not shown) of the bioimpedance taken for each single frequency f_i for each day.

The graphs thus obtained are compared, by the means for comparing, with further bioimpedance charts that describe a typical trend of the onset of a cardiopathy, not shown.

Is obtained then that, if by the comparison there is a correspondence between the two charts, i.e. that with the known trends and that obtained from the measurement on the patient, an onset of the cardiopathy can be diagnosed in order to prevent the cardiopathy.

In particular, the means for comparing compare the trend of the patient with the trend of the previous days t_1 , t_2 , t_n as well as with known data that are obtained from the clinical data of the patient 50. In this case, the comparison can be investigated also on the basis of such patient's clinical data which comprise for example fat mass index, age, sex, weight etc., to obtain a even higher reliability and then a more precise and accurate preliminary diagnosis.

On the basis of such multifrequency bioimpedance measurements, a cardiac decompensation or other cardiac diseases can be diagnosed in advance with respect to the

consequent diseases, in order to prevent them with appropriate therapies carried out on patient 50 under strict monitoring.

More in particular, as shown in Fig. 1, said means for analysing 40 comprises a sampling means 25 that is configured to operate the means for delivering 10 and the means for measuring 20 in a predetermined time range, in order to repeat a plurality of measurements at times t_1 , t_2 , t_n that are distant by said time range from each other. Structurally, the means for delivering 10 the electric stimulus comprises a couple of skin injection electrodes 11, 12 arranged at a distance from each other on the thorax of the patient 50, and a variable frequency electric generator 10 connected to the skin injection electrodes 11/12 and associated with the means 30 for adjusting the current stimulus. More precisely, the electric stimuli I_1 , I_2 , I_3 ... I_n are obtained starting from a variable frequency voltage generator $V(f)$ that represents the adjustment means 30. The variable frequency voltage thus obtained is then converted into the respective currents I_1 , I_2 , I_3 ... I_n at respective different frequencies f_1 , f_2 , f_3 ... f_n by a block 31.

In detail, the frequencies f_1 , f_2 , ... f_n are comprised in a range set between 1 kHz and a 1MHz and said electric stimuli have an intensity set between 0.1mA and 0.5mA, in particular 0.44mA.

Instead, the means for measuring 20 comprises a couple of skin sensor electrodes 21, 22 arranged substantially between the couple of injection electrodes 11, 12, as shown in Fig. 2, configured to measure a voltage V_{fi} tuned to the plurality of electric stimuli I_i at respective different frequencies f_i and a means for calculating 27 the module $|Z_i|$ of the bioimpedance as ratio between the absolute

values of the digital numerical series responsive to a voltage V_{fi} and the digital numerical series responsive to the current stimulus I_i at a predetermined frequency f_i , in order to obtain a corresponding digital numerical signal of the module Z of the bioimpedance (Fig.6).

In addition, as also shown in Fig. 6, the means for measuring 20 comprises a means 29 for calculating the phase PP_i of the bioimpedance as phase shift time Δt between the voltage V_{fi} and the current stimulus I_i at a predetermined frequency f_i , in order to obtain a corresponding signal P_i of the bioimpedance phase. Furthermore, as shown in Fig. 6, a means 29a for converting the signal of the phase PP_i of the bioimpedance into a respective digital numerical signal is provided. This way, the couple of skin sensor electrodes 21, 22 measure a voltage V_{f1} tuned to the current stimulus I_{f1} at frequency f_1 . By the ratio $V_{f1}/I_{f1}=Z_{f1}$ the module of the bioelectric impedance signal Z_{f1} relative to frequency f_1 can be obtained. Changing the frequency of the current I for a predetermined frequency band the modules of the bioimpedance signals $Z_{f1}, Z_{f2}, Z_{f3}, \dots Z_{fn}$ are obtained.

In the same way, for each voltage value V_{fi} tuned to the current stimulus I_{fi} at the respective frequency, the injected current signal I_{fi} is compared with the measured voltage signal V_{fi} taking into account the delay time Δt_i .

In particular, as shown in the diagrammatical view of Fig. 6, the current I_i is generated starting from a predetermined digital numerical series, then turned into analog signal by a digital-analog converter, and eventually transformed from voltage to current which is supplied to injection electrodes 11, 12. On the other hand, sensor electrodes 21, 22 detect a corresponding voltage that passes through a filter and then through a signal amplifier

and eventually through a digital-analog converter for making a corresponding voltage digital signal.

The bioimpedance module is obtained by combining the digital signals of current I_i and of voltage V_i . To obtain
5 the phase P the phase shift time is measured between the analog signal of the injected current and the analog signal relative to the measured voltage. Such phase shift, which is the bioimpedance phase, is then encoded into a digital signal for assisting the computing steps.

10 More in particular, the steps of computing the module and the phase of each complex bioimpedance signal Z_i are made, as shown in Fig. 6, by means of respective analog and/or digital demodulator electronic circuits 27/29, among which a divider block for the module and a phase detector for the
15 phase, from which the respective digital signals of the module Z and of the phase P_i exit as output. In an advantageous way, the means for calculating the module and the phase comprises, furthermore, a signal amplifier 28 and a band pass filter 26 accordable in frequency.

20 Such a multifrequency measurement of the bioimpedance is used, furthermore, to obtain hemodynamic signals, i.e. data on cardiac parameters that can be compared and combined with the monitoring results obtained as above described.

In particular, such hemodynamic signals are obtained from
25 a higher sampling frequency, for example 200 samples per second for a time of 1 minute, and from a computing step, by means of known algorithms of curves representing said signals (Fig.4 and 5). The sampling, i.e. detecting the plurality of complex signals, on both module and phase, of
30 the bioimpedance, and the parameters from it obtained, are in this case instantaneous.

In other words, the means for analysing 40 comprises a plurality of known algorithms for extracting, from the

bioimpedance complex signal, cardiovascular hemodynamic functionality signals, like the cardiac output (volume-minute), the cardiac index, the stroke volume, the system vascular resistance, the flow acceleration index, the flow velocity index, the thoracic fluid content, the cardiac work, the pre-ejection time and ventricular ejection time etc.

Furthermore, said means for analysing 40 is configured to compare the cardiovascular hemodynamic functionality signals with the time chart of the bioimpedance measurement, to obtain a more reliable prediction of said cardiopathy.

Through multifrequency device 100, according to the invention, the above described parameters are calculated not on the basis of a signal detected at a single frequency, but on the basis of a plurality of signals measured at different frequencies.

Such solution allows to overcome the difficulties of the known devices that require a hospitalisation, specialized operators for applying the electrodes, and laying steadily the patient 50 on a special plane support.

The multifrequency device, according to the invention, allows instead a practical usage that enables the patient 50 a simple and direct application of the device same.

In other words, a peculiar element of device 100 with respect to the known devices consists of applying such algorithms not only to a bioelectric impedance signal (bioimpedance module) acquired at a predetermined frequency, but also of applying them to a plurality of signals taken at different frequencies. This way a set of values of the hemodynamic variables is generated for each frequency of the stimulation signal. By comparing and computing such numerical set reliable values of the

hemodynamic variables of the patient are obtained, even with a wearable device.

If some hemodynamic variables obtained at determined frequencies turn out with values higher or less than determined thresholds, the multifrequency monitoring allows, in fact, to generate for example a positioning error signal of the electrodes and then to warn the patient that an alarm threshold has been exceeded.

In particular, as shown in the diagrammatical view of Fig. 7, by the bioimpedance multifrequency data Z_i , relative both to the module and the phase, measured on the patient 50, and by their comparison using an algorithmic "merging", hemodynamic signals are obtained responsive to the frequency f_i .

Such hemodynamic signals can be further computed and integrated on the basis of the clinical data of the same patient 50 to obtain a realistic and reliable value.

Finally, by combining the hemodynamic variables thus obtained with the comparison of the multi frequential complex pattern of the bioimpedance with known charts and trends which are relative to situations of cardiopathy, it is possible to obtain an early diagnosis in a way reliable using a wearable device and of easy use.

In a preferred exemplary embodiment, as shown in Fig. 8, the couple of injection electrodes 11, 12 and the couple of sensor electrodes 21, 22 are substantially arranged in line, in particular they can be associated with a belt or other wearable element 60. This way, the relative position of the electrodes remains fixed, in order to reduce the artifacts of the measurement due to a wrong or inaccurate positioning.

In particular, the device further comprises an interface means that is configured to transfer the collected and

computed data to a central collection and correlation unit which can correlate it with other signals. The interface means is for example a wireless or wired interface or, alternatively, a coupling means that is arranged to provide
5 a matching shape with the central collection unit 200, as shown in Fig. 8.

In case of a wireless interface or an interface with matching shape device 100 is wearable and is configured to monitor the patient 50 for a long period, for example 24h
10 or for more days.

In a further application, the interface means can be used for combining device 100 with other sensor devices and modules such as an accelerometer, an electrocardiograph, a device for pulse oximetry that measures the oxygen
15 concentration in the blood, a module for measuring the pressure, the temperature etc.

The foregoing description of an embodiment of the method and of the apparatus according to the invention will so fully reveal the invention according to the conceptual
20 point of view, so that others, by applying current knowledge, will be able to modify and/or adapt for various applications such embodiment without further research and without parting from the invention, and it is therefore to be understood that such adaptations and modifications will
25 have to be considered as equivalent to the specific embodiment. The means and the materials to realise the different functions described herein could have a different nature without, for this reason, departing from the field of the invention. It is to be understood that the
30 phraseology or terminology the is employed herein is for the purpose of description and not of limitation.

CLAIMS

1. A early diagnosis device (100) in a patient (50) for cardiopathies such as a cardiac decompensation and/or cardiovascular diseases which can be determined by detecting hemodynamic variables of the patient (50), said early diagnosis device (100) comprising:

- a wearable support (1);
- a diagnostic unit (5) mounted to said wearable support (1), said diagnostic unit (5) comprising:

- a means for delivering (10) an electric stimulus I_i at a predetermined frequency f_i to the body of said patient (50),

- a means for measuring (20) a thoracic electrical bioimpedance Z_i in the body of said patient (50) by providing a bioelectric impedance signal on the basis of said electric stimulus I_i at said predetermined frequency f_i ;

- an adjustment means (30) for adjusting said frequency of said electric stimulus I_i such that a plurality of electric stimuli is delivered $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, \dots f_n$, said means for measuring (20) the thoracic electrical bioimpedance Z_i configured to measure a corresponding complex bioimpedance signal $Z_1, Z_2, Z_3 \dots Z_n$ for each of said plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, \dots f_n$, and to provide a plurality of complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$;

- a memory (35) that is configured to store said plurality of complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ at a first time t_1 , at a second time t_2 and at

an nth time t_n ;

- a means for extracting the real part $R_1, R_2, R_3 \dots R_n$ of said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ recorded in said memory at said first time t_1 ,
5 second time t_2 and nth time t_n , to obtain a respective time chart C_1, C_2, C_n of said real part for each frequency $f_1, f_2, \dots f_n$ at the times $t_{(1)}, t_{(2)}, \dots t_n$;
- a means for analysing (40) said time chart C_1, C_2, C_n of said real part $R_1, R_2, R_3 \dots R_n$, in order to
10 obtain a decrease rate with time of said real part for each frequency $f_1, f_2, \dots f_n$ and to calculate a decrease value DR/Dt ;
- an alarm means to provide an alarm (46) of cardiac
15 decompensation associated with said means for analysing (40), said alarm generated if said decrease value DR/Dt is higher than a predetermined value DR_0/Dt .

2. A device, according to claim 1, wherein said means for
20 analysing (40) comprises a sampling means (25) that is adapted to operate said means for delivering (10) and said means for measuring (20) in a predetermined time range, in order to repeat a plurality of said bioimpedance measurements at times $t_1, t_2, \dots t_n$ that are
25 distant said time range from each other.

3. A device, according to claim 2, wherein said sampling time range is one day, and said number n of times $t_1, t_2, \dots t_n$ is set between 7 and 30 days, preferably 14 days.

30 4. A device, according to claim 1, wherein said means for analysing (40) is configured to compare said decrease value DR/Dt obtained from a time chart of the real part $R_1, R_2, R_3 \dots R_n$ of the complex bioimpedance signals

determined on the patient (50) also with characteristic time charts of a cardiopathy that is adapted by means of clinical data of said patient (50), in order to increase the amount of data for comparison and to obtain a more precise prediction, in particular said clinical data describing the health status of the patient and being selected from the group consisting of: age, sex, weight, fat-free mass index, etc.

5. A device, according to claim 1, wherein said means to provide an alarm (46) comprise an acoustic emitter.

6. A device, according to claim 1, wherein the following are further provided:

- a means for extracting the imaginary part $L_1, L_2, L_3 \dots L_n$ of said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ to obtain a respective time chart of said imaginary part for each frequency $f_1, f_2, \dots f_n$ at the times $t_{(1)}, t_{(2)}, \dots t_n$;

- a means for analysing (40) said time chart of said imaginary part $L_1, L_2, L_3 \dots L_n$, in order to obtain a rate of variation with time of said imaginary part for each frequency $f_1, f_2, \dots f_n$ and to calculate a variation value DL/Dt ;

- a means to provide a cardiac decompensation parameter associated with said means for analysing (40) if said variation value DL/Dt exceeds the limits by a predetermined range.

7. A device, according to claim 1, wherein said complex bioimpedance signals $Z_1, Z_2, Z_3 \dots Z_n$ are calculated as average values within a predetermined measurement range, in particular set between 3 and 10 minutes.

8. A device, according to claim 1, wherein said means for delivering (10) an electric stimulus I_i deliver a electric current stimulus and comprises:

- a couple of skin injection electrodes (11, 12) at a distance from each other and arranged on the thorax of said patient (50);
- a variable current frequency generator (10) connected to said skin injection electrodes (11, 12) and associated with said adjustment means (30) that adjust said current stimulus I_i , such that said adjustment means (30) controls in frequency said current generator (10) such that it injects said plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, f_3 \dots f_n$ said current having a corresponding predetermined digital numerical series.

9. A device, according to claim 1, wherein said different frequencies $f_1, f_2, \dots, f_n$ are comprised in a range set between 1 kHz and a 1 MHz and said electric stimuli $I_1, I_2, I_3 \dots I_n$ of current have an intensity set between 0.1mA and 0.5mA, in particular 0.44mA.

10. A device, according to claim 1, wherein said means for measuring (20) comprises:

- a couple of skin sensor electrodes (21, 22) arranged substantially between said couple of injection electrodes (11, 12), said couple of skin sensor electrodes (21, 22) configured to measure a voltage V_{fi} tuned to said plurality of electric stimuli $I_1, I_2, I_3 \dots I_n$ at respective different frequencies $f_1, f_2, \dots, f_n$;
- a means for transforming said voltage into a digital numerical series;
- a means for calculating (27) the module $|Z_i|$ of the bioimpedance as a ratio between the absolute values of said digital numerical series responsive to said voltage V_{fi} and of said digital numerical series

responsive to said current stimulus I_i at a predetermined frequency f_i , in order to obtain a corresponding digital numerical signal of the module Z of the bioimpedance;

5 - a means for calculating (29) the phase P_i of the bioimpedance as phase shift time Δt between said voltage V_{fi} and said current stimulus I_i at a predetermined frequency f_i , in order to obtain a corresponding signal of the bioimpedance phase;

10 - a means for converting (29a) said signal of the phase P_i of the bioimpedance into a respective digital numerical signal.

11. A device, according to claim 1, wherein said means for analysing (40) comprises:

15 - an programmable logic unit (45) that contains said means for analysing;
- said memory (35) connected to said programmable logic unit (45);

wherein said programmable logic unit (45) is associated
20 with said sampling means (25), with said means for delivering (10) and with said means for measuring (20) in order to select a predetermined frequency f_i of said electric stimulus I_i for generating and analysing said plurality of complex bioimpedance signals, in particular
25 for generating and analysing the modulus and phase signals at said different frequencies $f_1, f_2, \dots, f_n$ in a way to generate said time chart C_1, C_2, C_n and compare it with a time chart present in said memory (35).

12. A device, according to claim 1, wherein said means for
30 analysing (40) is further configured to extract the from said complex bioimpedance signals, cardiovascular hemodynamic functionality signals like a cardiac output (volume-minute), a cardiac index, a stroke volume, a

system vascular resistance, a flow acceleration index, a flow velocity index, the thoracic fluid content, a cardiac work, the pre-ejection time and ventricular ejection time etc., in particular, said hemodynamic signals obtained from a sampling at high frequency, in particular 200 samples per second for a predetermined time.

13. A device, according to claims 1 and 3, wherein said means for analysing (40) is configured to compare said cardiovascular hemodynamic functionality signals with said time chart to obtain a more reliable prediction of said cardiopathy.

14. A device, according to claim 1, wherein said device (100) further comprises an interface means that is adapted to transfer the collected and computed data to a central collection and correlation unit (200) for correlation with other signals, in particular said interface means is a wireless or wired interface means, in particular said interface means can be used for combining the device with other sensor devices and modules, such as an accelerometer, an ECG, a device for pulse oximetry that measures the oxygen concentration in the blood, a module for measuring the pressure, the temperature etc.

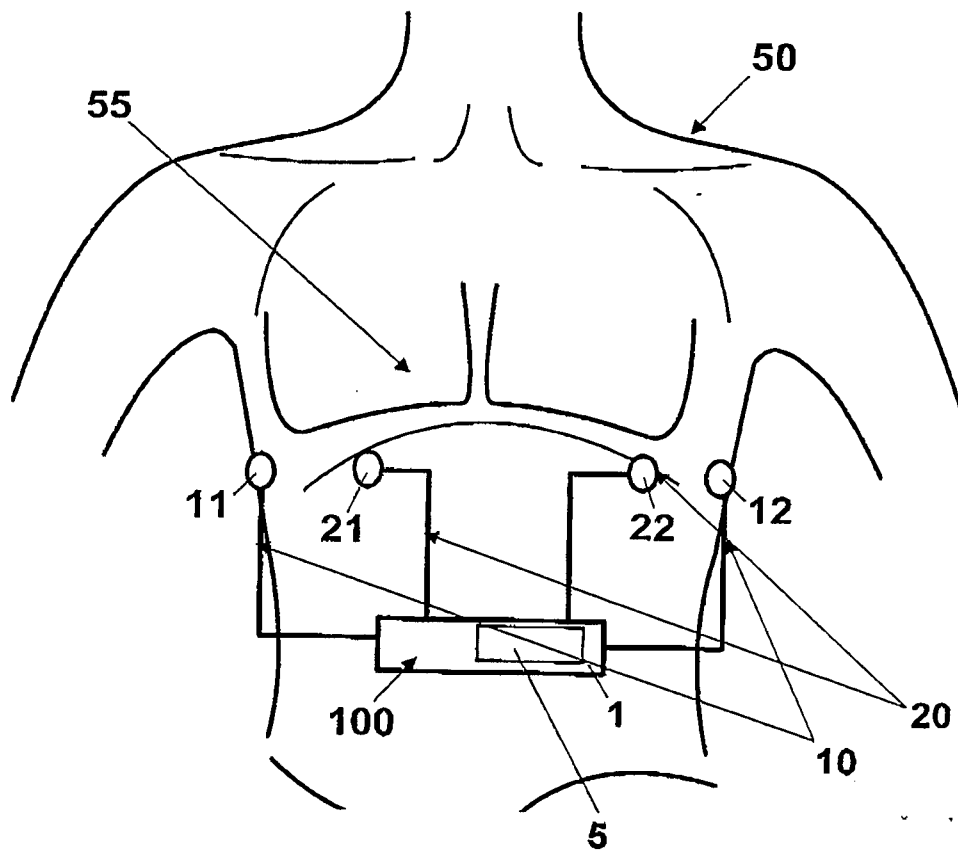
Fig. 2

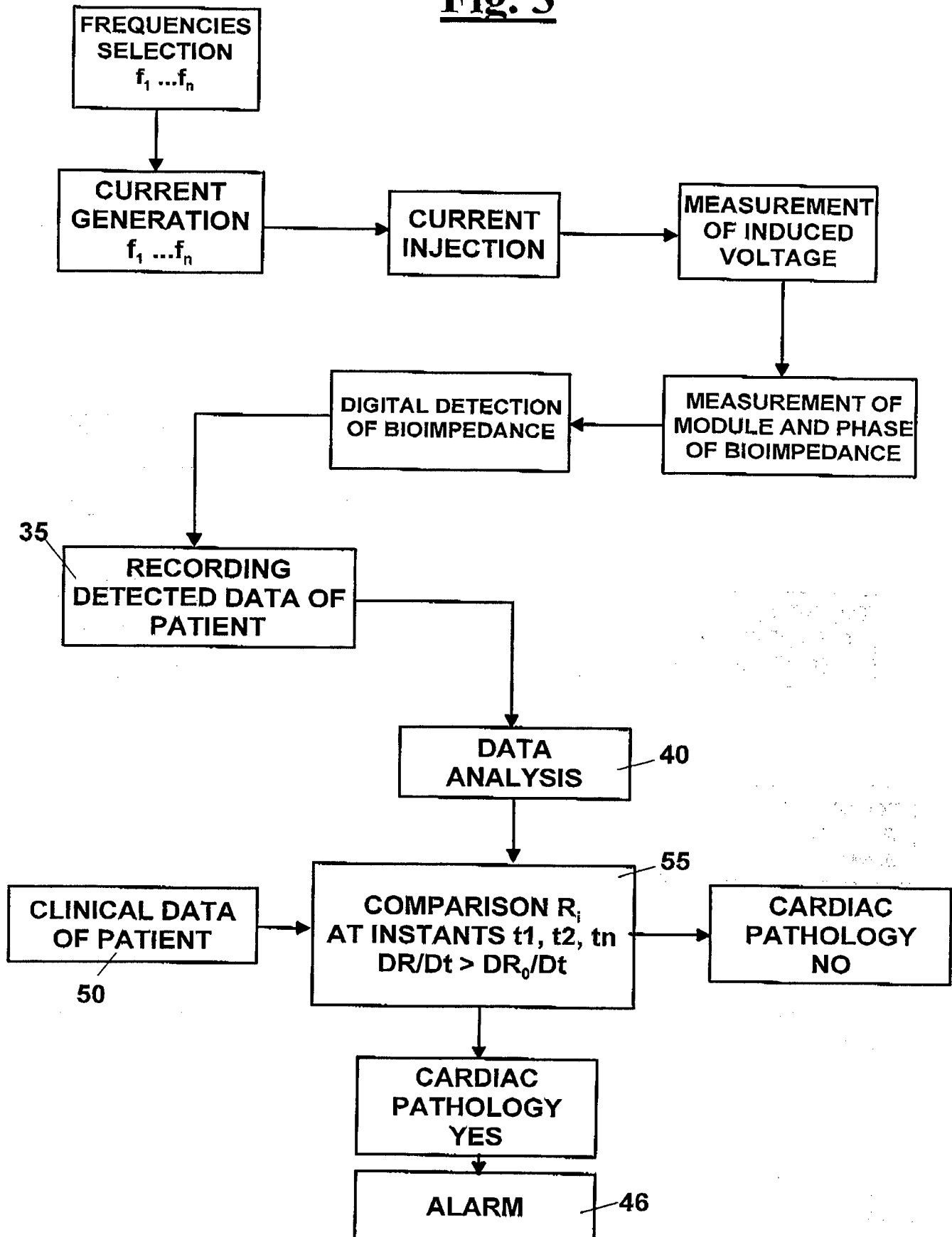
Fig. 3

Fig. 3A

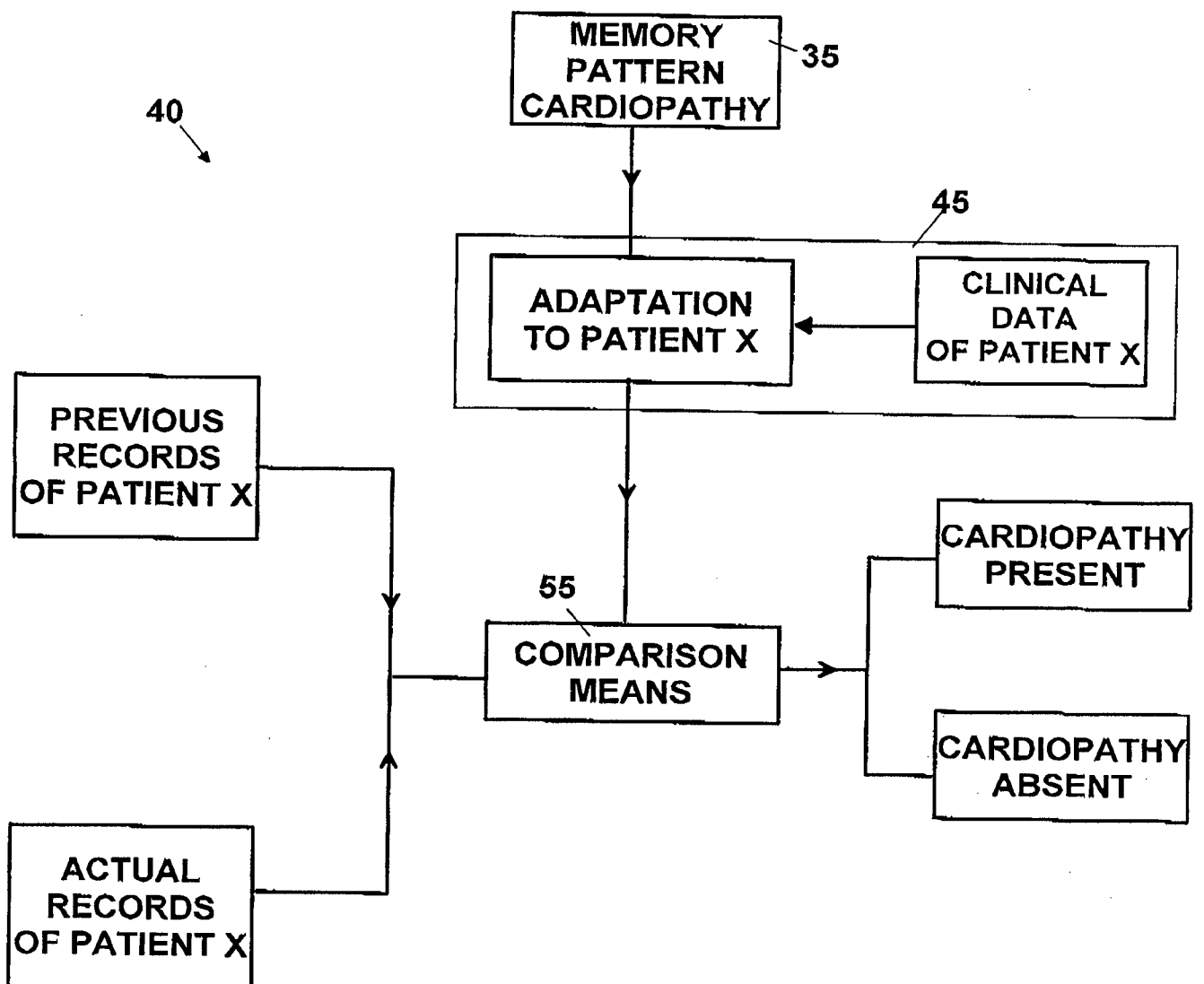


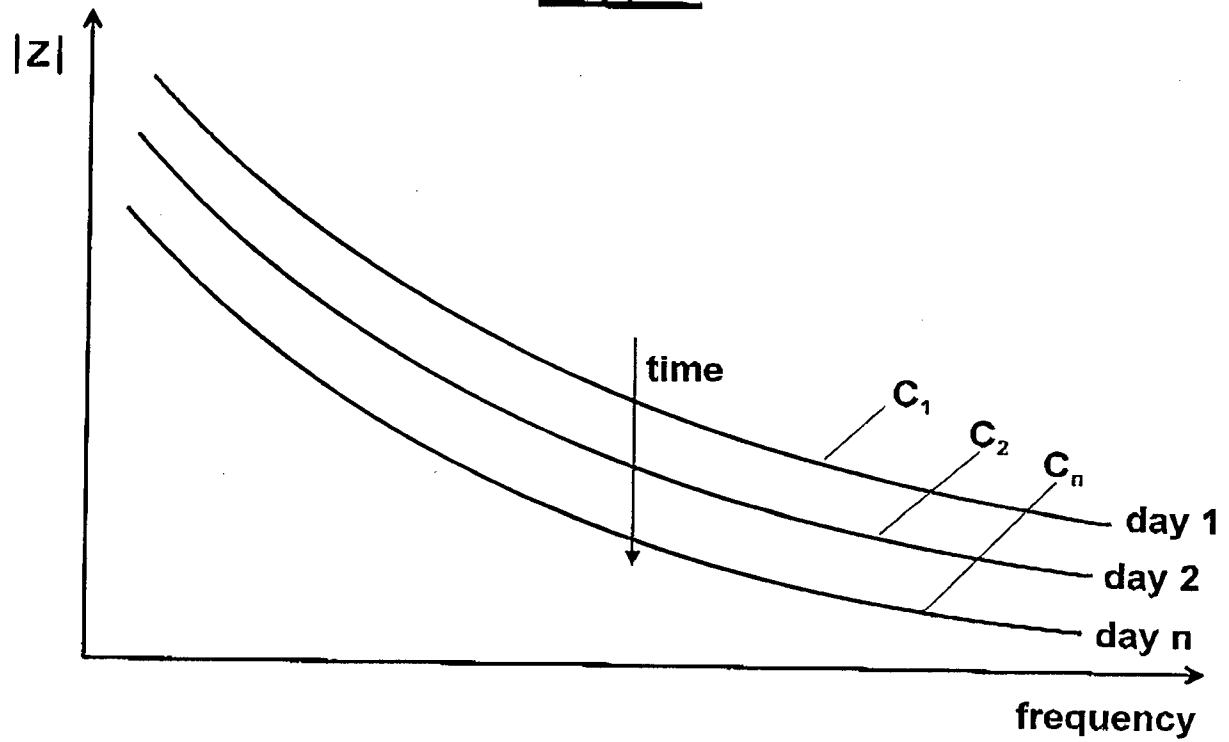
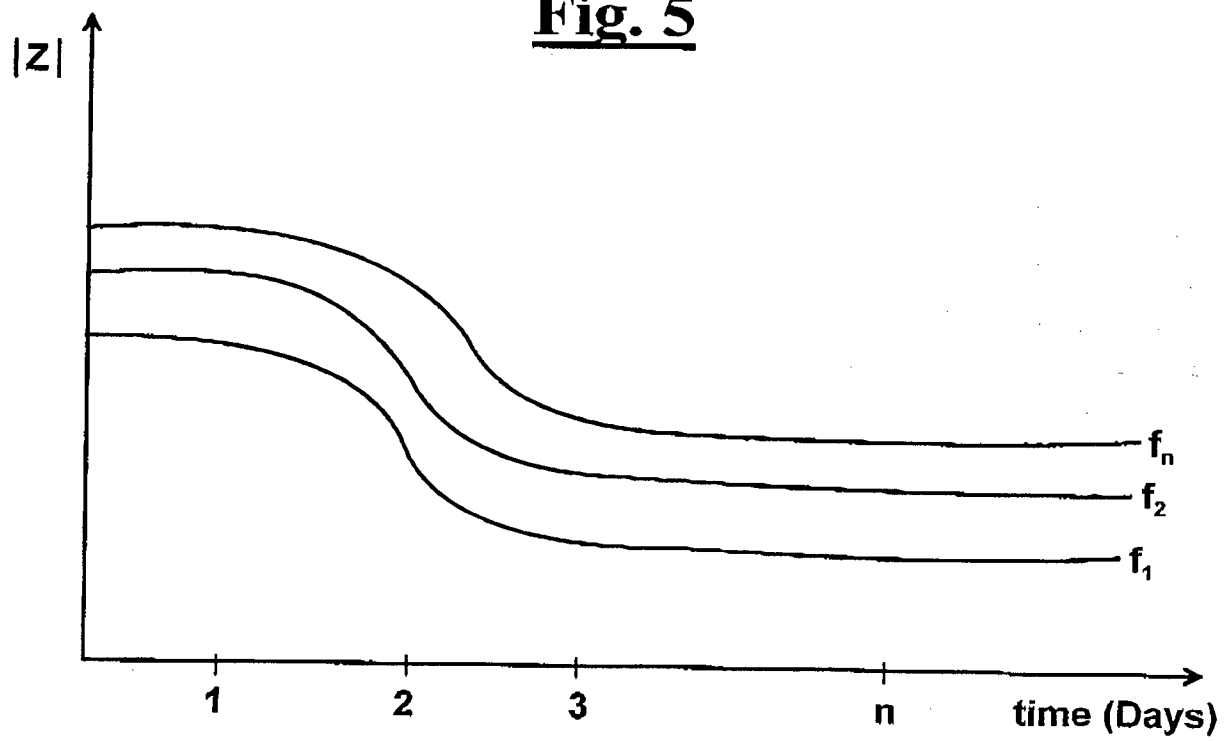
Fig. 4**Fig. 5**

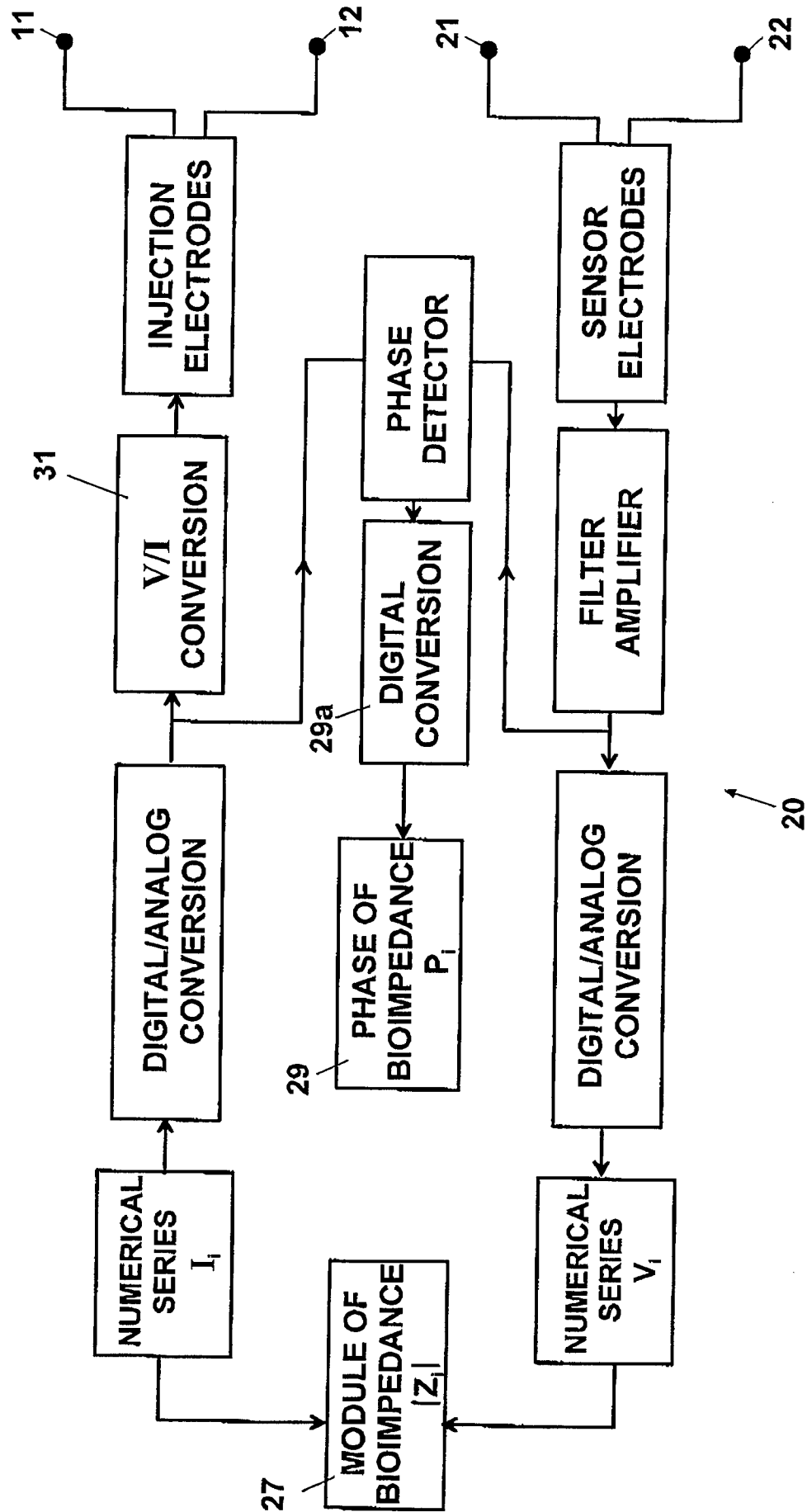
Fig. 6

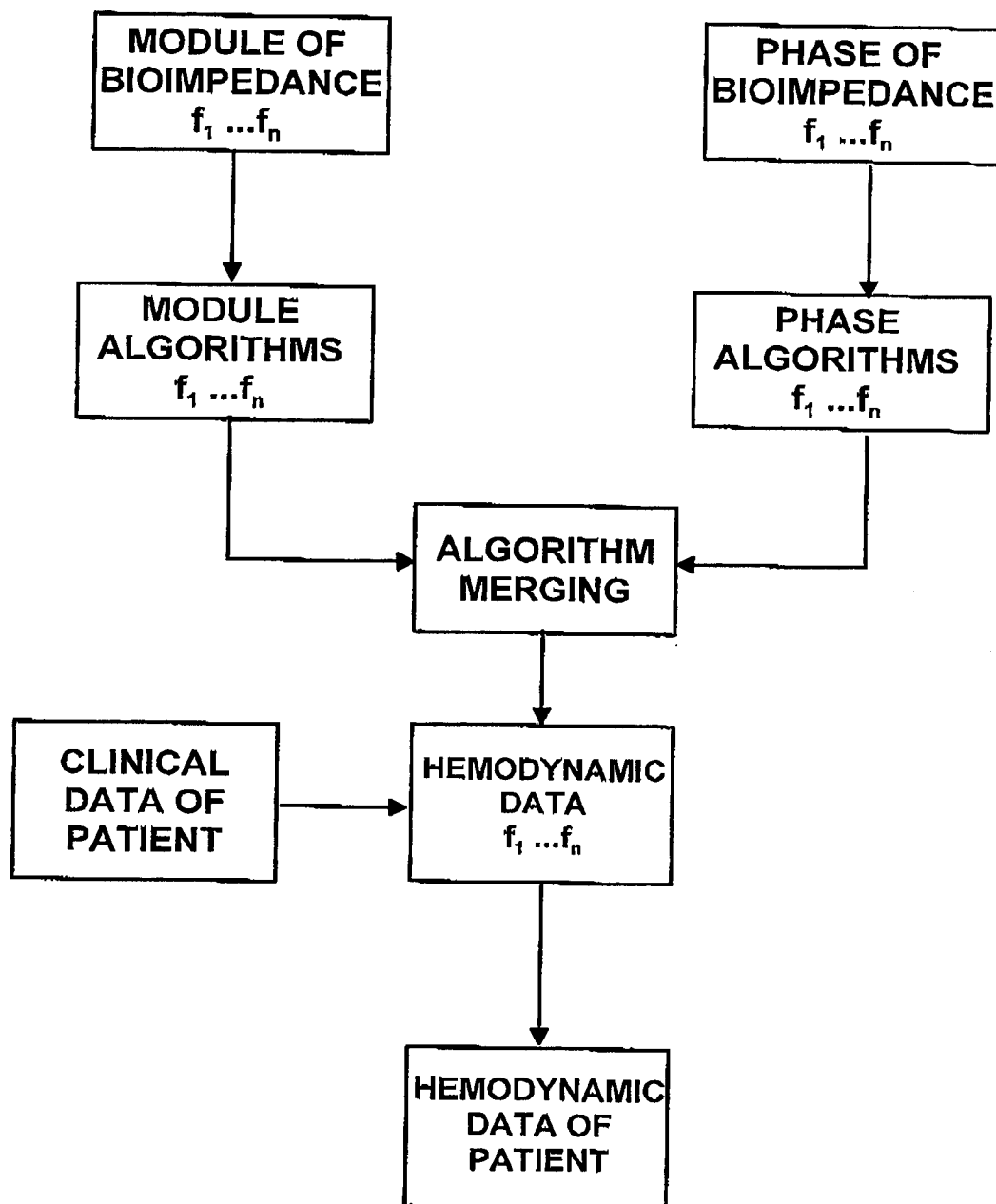
Fig. 7

Fig. 8