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(54) Title: A METHOD AND SYSTEM FOR ANALYZING AN ELECTROCARDIOGRAPHIC SIGNAL

(57) Abstract: A method for analyzing an ECG signal includes obtaining a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal and detecting an altered ventricular repolarization based on the obtained measured area based repolarization interval.

A METHOD AND SYSTEM FOR ANALYZING AN ELECTROCARDIOGRAPHIC SIGNAL

[0001] This application claims the benefit of U.S. Provisional Patent Application Serial No. 60/311,921 filed August 13, 2001 which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention is directed to a method and system for the quantification of repolarization changes when measured in a dynamic electrocardiogram ("ECG") signal.

BACKGROUND OF THE INVENTION

[0003] An ECG signal represents changes in electrical potential produced by contractions of the heart recorded from the surface of the body. An example of an ECG signal is illustrated in FIG. 1. Each P-QRS-T complex reflects the electrical depolarization and repolarization components of the heart beat. The cardiac beat comprises three major waves identified as: the P wave representing the depolarization of the auricles, the QRS complex generated by the depolarization of both right and left ventricles, and the T-wave which represents the repolarization of the ventricles. The T wave also includes an apex, T_{apex}, and an endpoint, T_{offset}. The repolarization of the auricles is hidden in the QRS complex. The RR intervals are defined by the interval between two consecutive R peaks in successive beats. The RR interval is a direct measurement of the heart rate.

[0004] In an ECG signal, a modification of the T wave morphology can be observed when certain pharmaceutical agents are taken and also with certain types of cardiac disorders. In particular, it is known that prolongation of the QT interval in an ECG signal is clearly associated with an increased risk for ventricular arrhythmias and sudden cardiac death. Accordingly, prior systems have been developed to monitor the QT interval in ECG signals to detect potential heart problems.

[0005] Although these prior systems work, they have problems in accurately identifying the endpoint of the T wave when the endpoint of the T wave gradually approaches the baseline, when a U wave is present, or when the shape of T wave is biphasic. If the apex or the endpoint of the T wave are not accurately identified, the accuracy and robustness of repolarization analysis, i.e. analysis of the QT interval, especially with dynamic ECG signals, such as those obtained by exercise ECG testing, is compromised.

SUMMARY OF THE INVENTION

[0006] A method and a computer readable medium with programmed instructions for analyzing an ECG signal in accordance with an embodiment of the present invention includes obtaining a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal and detecting an altered ventricular repolarization based on the obtained measured area based repolarization interval.

[0007] A system for analyzing an ECG signal in accordance with an embodiment of the present invention includes a measurement system and a detection system. The measurement system obtains a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal. The detection system detects an altered ventricular repolarization based on the obtained measured area based repolarization interval.

[0008] A method and a computer readable medium with programmed instructions for analyzing an effect of a pharmacological agent on an electrocardiogram signal in accordance with an embodiment of the present invention includes obtaining a first measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal. The pharmacological agent is administered. A second measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal is obtained from at least one of a first period during which the pharmacological agent is in effect and a second period after the pharmacological agent is no longer

in effect. An altered ventricular repolarization is detected based on the first and second measurements.

[0009] A system for analyzing an effect of a pharmacological agent on an electrocardiogram signal in accordance with an embodiment of the present invention includes a measurement system and a detection system. The measurement system obtains a first measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal before administering the pharmacological agent. The measurement system also obtains a second measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal from at least one of a first period during which the pharmacological agent is in effect and a second period after the pharmacological agent is no longer in effect. The detection system detects an altered ventricular repolarization based on the first and second measurements.

[0010] The present invention provides an effective non-invasive method for dynamic quantification of ventricular repolarization. The present invention's comprehensive evaluation of ventricular repolarization provides enhanced utility: in the clinical diagnosis of acquired and inherited repolarization disorders; in the evaluation of new chemical entities for pharmaceutical companies during drug development and during post-marketing surveillance of approved drugs that can adversely affect ventricular repolarization; and in the clinical identification of patients with potentially life-threatening ventricular repolarization disorders, such as those after myocardial infarction.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 is a diagram of a beat in an ECG signal where two vertical lines mark the apex and the offset of the T wave used to measure QT intervals;

[0012] FIG. 2 is a block diagram of a quantification system in accordance with one embodiment of the present invention;

[0013] FIG. 3A is a diagram of another ECG signal;

[0014] FIG. 3B is a graph of a normalized absolute integral of the repolarization segment of the ECG signal shown in FIG. 3A;

[0015] FIG. 4 is a flow chart of a method for analyzing an ECG signal in accordance with another embodiment of the present invention;

[0016] FIGS. 5A-5C are graphs of the magnitude, phase, and zeros and poles of a filter for the quantification system;

[0017] FIG. 6A is a graph of six area based repolarization intervals of median beats which are superimposed;

[0018] FIG. 6B is a graph of cumulative area of the six area based repolarization intervals shown in FIG. 6A;

[0019] FIG. 7 is a table of RTx% and RR interval bins;

[0020] FIG. 8A is a graph of a heart rate of one patient showing beats per minute (BPM) against time;

[0021] FIG. 8B is a graph of a RT intervals (Apex and offset of T waves using median value across leads) of the one patient;

[0022] FIGS. 9A-9D are graphs of trends for T-wave amplitude for the median across leads, the X leads, the Y leads, and the Z leads;

[0023] FIGS. 10A-10D are graphs of the trends for area-based measurements for 25% of the area for the median, , the X leads, the Y leads, and the Z leads;

[0024] FIGS. 11A-11D are graphs of the trends for area-based measurements for 50% of the area for the median, , the X leads, the Y leads, and the Z leads;

[0025] FIGS. 12A-12D are graphs of the trends for area-based measurements for 90% of the area for the median, , the X leads, the Y leads, and the Z leads;

[0026] FIGS. 13A-13D are graphs of the trends for area-based measurements for 97% of the area for the median, , the X leads, the Y leads, and the Z leads;

[0027] FIG. 14 is a table of averages for 24 hours, during the day and at night for: beats per minute (BPM); X, Y, and Z amplitudes; X RT apex, Y RT apex, and Z RT apex; X RT offset, Y RT offset, and Z RT offset; XT 25% area, YT 25% area and ZT 25% area; XT 50% area, YT 50% area and ZT 50%; area XT 90% area, YT 90% area and ZT 90%; and area XT 97% area, YT 97% area and ZT 97% area;

[0028] FIG. 15 is an hourly table of heart rate (BPM), T wave ampl X, T wave ampl Y, and T wave ampl Z;

[0029] FIG. 16 is an hourly table of heart rate (BPM), T wave apex X, T wave apex Y, and T wave apex Z;

[0030] FIG. 17 is an hourly table of heart rate (BPM), T wave offset lead X, T wave offset lead Y, and T wave offset lead Z;

[0031] FIG. 18 is an hourly table of heart rate (BPM), ABRI RT25 X-lead, ABRI RT25 Y-lead, and ABRI RT25 Z-lead;

[0032] FIG. 19 is an hourly table of heart rate (BPM), ABRI RT50 X-lead, ABRI RT50 Y-lead, and ABRI RT50 Z-lead;

[0033] FIG. 20 is an hourly table of heart rate (BPM), ABRI RT90 X-lead, ABRI RT90 Y-lead, and ABRI RT90 Z-lead;

[0034] FIG. 21 is an hourly table of heart rate (BPM), ABRI RT97X-lead, ABRI RT97 Y-lead, and ABRI RT97 Z-lead;

[0035] FIGS. 22A-22B are graphs of PointCarre plots over 24-hours of RT offset=f(RR) (median across leads) and RT apex=f(RR) (median across leads);

[0036] FIGS. 23A-23B are graphs of PointCarre plots over 24-hours of RT area 25%=f(RR) (median across leads) and RT area 50%=f(RR) (median across leads); and

[0037] FIGS. 24A-24B are graphs of PointCarre plots over 24-hours of RT area 90%=f(RR) (median across leads) and RT area 97%=f(RR) (median across leads).

DETAILED DESCRIPTION

[0038] A system 10 and method for analyzing an ECG signal in accordance with one embodiment of the present invention are illustrated in FIGS. 2 and 4. In this particular embodiment, the system 10 includes a quantification system 12 coupled to an ECG device 24 and a storage device 26. The method includes filtering and then extracting a portion of the filtered ECG signal, substantially removing any baseline from the extracted portion of the ECG signal, obtaining a measurement of at least one area based repolarization interval in the extracted portion, and then detecting any altered ventricular repolarization based on the measured area based repolarization interval. The present invention provides a number of advantages including providing an effective non-invasive method for dynamic quantification of ventricular repolarization.

[0039] Referring to FIG. 2, the quantification system 12 has a central processing unit ("CPU") or processor 14, a memory 16, an input/output interface

22, a display 18, and a user input device 20 which are coupled together by a bus system 23 or other link, although the quantification system 12 may comprise other types of components, other numbers of the components, and other combinations of the components. The processor 14 executes a program of stored instructions for at least a portion of the method for analyzing an ECG signal in accordance with one embodiment of the present invention as described herein. In this particular embodiment, the preprocessing and processing steps are carried out by quantification system 12, although other types and combinations of systems and/or devices can be used to execute the preprocessing and processing steps.

[0040] Memory 16 comprises a random access memory (RAM) and a read only memory (ROM), although other types and combinations of memory storage devices can be used, such as a floppy disk, hard disk, CD ROM, or other computer readable medium which is read from and/or written to by a magnetic, optical, or other reading and/or writing system that is coupled to the processor 14. Although in his particular embodiment, the method in accordance with one embodiment of the present invention is stored as programmed instructions in memory 16 in the quantification system 12 for execution by the processor 14, some or all of the programmed instructions could be stored elsewhere.

[0041] The display 18 enables an operator to observe information, such as the ECG reading for a patient. In this particular embodiment, the display 18 is a cathode ray tube device, although other types of displays can be used, such as a printer.

[0042] The user input device 20 enables an operator to generate and transmit signals or commands to the processor, such as a request to obtain or retrieve ECG signals for a particular patient for processing. In this particular embodiment, the user input device 20 is a keyboard, although other types of user input devices can be used, such as a computer mouse.

[0043] The input/output interface 22 is used to operatively couple the quantification system 12 to the ECG device 24 and the storage device 26, although

quantification system 12 can be coupled via input/output interface to other systems and/or devices.

[0044] The ECG device 24 records one or more ECG signals from one or more patients. The ECG device can capture the electrical activity from the heart in a variety of different manners, such as Holter recordings, exercise ECG testing, bedside ECG monitoring, event monitoring, implantable ECG recorders using one or more leads and with a duration that may vary from few minutes to twenty-four hours, even few days. A variety of different types of ECG devices can be used for ECG device 24. The ECG information can be transmitted to the quantification system 12 from the ECG device 24 for processing.

[0045] The storage device 26 comprises a RAM, although other types and combinations of memory storage devices can be used, such as a ROM or a floppy disk, hard disk, CD ROM, or other computer readable medium which is read from and/or written to by a magnetic, optical, or other reading and/or writing system. The storage device 26 can store ECG readings for processing by the quantification system 12 and can store the results of any processing.

[0046] Referring to FIG. 3A, an example of another ECG signal is illustrated. In this particular example, the Q peak is reached at time Q_0, the T wave begins at time S_0, the T apex is reached at T_m, and the endpoint of the T wave is reached at T_o.

[0047] Referring to FIG. 3B, a graph of the measured area under the repolarization interval shown in FIG. 3A with the Y axis showing the percentage of the total area under the repolarization interval and the X-axis showing time is illustrated. The graph begins at time S_0 which again corresponds to the time when the T wave begins and U_0 represents the time when substantially 100% of the area under the repolarization area is measured. The times to accumulate 25%, 50% and 75% of the absolute T-wave area are identified as LA25, LA50, LA75, respectively. Unlike prior systems, the present invention does not rely upon accurately determining either the T apex, T_m, or the endpoint of the T wave, T_o.

Instead, the present system identify the end of the T wave when the slope of the repolarization signal is below a given threshold. The present invention quantifies changes in ventricular repolarization based on measurements of the area under the repolarization interval obtained starting at a time S_0, which is a first period of time after the R peak is detected.

[0048] The morphology of the repolarization T wave in an ECG signal, such as the one shown in FIG. 3A, can be influenced by any factor that alters ion-channel kinetics involved in ventricular repolarization, including inherited diseases, acquired cardiac diseases, metabolic disturbances, and drugs. Since the normal morphology of the ventricular repolarization interval is well known to those of ordinary skill in the art, an altered or abnormal morphology ventricular repolarization interval can be both visually and quantitatively assessed if it is accurately measured. A process for analyzing ventricular repolarization in accordance with the present invention is described below.

[0049] Referring to FIGS. 2, 3A, 3B, and 4, a method for analyzing an ECG signal in accordance with one embodiment is described below. Beginning in step 28, the quantification system 12 obtains an ECG signal or signals. The ECG signals can be obtained from a variety of different sources, such as directly from the ECG device 24 or from the storage device 26 which stores previously recorded ECG signals.

[0050] In step 30, the ECG signal undergoes low pass-filtering in quantification system 12. The filtering technique used should preserve the initial shape of the T wave. In this particular embodiment, the ECG signal is filtered in the forward direction, the filtered ECG signal is then reversed and run back through the filter again. The result of this filtering operation has precisely zero phase distortion and magnitude modified by the square of the filter's magnitude response.

[0051] By way of example only, in this particular embodiment a Butterworth filter and a bidirectional filtering technique are used in order to obtain

a high quality filtering free of distorted components, although other types of filters and filtering techniques can be used. In this example, a filter of order two with a cutoff frequency at -3db equal to 18 Hz is used. Graphs of the magnitude, phase (radians) and zeros and poles of this filter used for removing noise components of the ECG signal and reducing morphological changes of area based repolarization interval are illustrated in FIGS. 5A-5C.

[0052] Referring back to FIG. 4, in step 32 a portion or limited length sequence of the filtered ECG signal is extracted by the quantification system 12. More specifically, the ECG signal is cut into portions or sequences of consecutive continuous beats by quantification system 12, excluding non-normal beats. In each of these portions, $R(k)$ is the R peak location in the k^{th} beat in each portion and $ECG(n)$ is the n^{th} portion of ECG signal where n represents the number of portions of the ECG signal. Each ECG portion which is analyzed is $ECG(n)$ for $n \varepsilon [R(k), R(k + NB)]$ where NB is the number of beats in each analyzed interval. In this example, a repolarization segment is extracted for each of seventy consecutive beats in the filtered ECG signal.

[0053] In step 33, the baseline B(k) of the extracted portion of the ECG signal $ECG(n)$ is substantially removed by the quantification system 12. The baseline removal must be accurate and must avoid adding significant components to the repolarization segment in the ECG signal $ECG(n)$. By way of example only, in this particular embodiment the baseline removal can be obtained based using a Cubic-Spline interpolation of the baseline of the ECG signal $ECG(n)$, although other techniques for removing the baseline can be used. The interpolation used in this particular example is based on the average amplitude value of the samples from a limited squared time window $W(n)$ of 80 ms length located just before the beginning of the QRS complex. $B(k)$ is defined such as: $B(k) = ECG(R(k)-16)$ for a signal at 200 Hz sampling frequency. The signal $B(k)$ is interpolated at a sampling period equal to the sampling period of the ECG. The Cubic Spline interpolation of $B(k)$ is used to insure continuous smoothness up to the second derivative and is less likely to generate erratic oscillations than polynomial interpolation. The interpolated curve, corresponding to the very low

components of the ECG signal $ECG(n)$, is subtracted from the ECG signal $ECG(n)$ in order to reduce the effect of respiratory components of the signal. After subtracting the estimated baseline, two beats are removed from the beginning and two beats from the end of the analyzed intervals in the ECG signal $ECG(n)$. In this particular example, two beats are removed from the extremities of the ECG signal with seventy beats resulting in sixty-six beats which are analyzed. This insures elimination of undesirable side effects of the Cubic Spline interpolation that may occur at the beginning and the end of the analyzed portion of the ECG signal $ECG(n)$ which may alter the morphology of T wave;

[0054] In step 34, the portion of the ECG signal $ECG(n)$ with the baseline removed is now subjected to beat filtering to remove non-normal beats from the analysis by quantification system 12. No interpolation of the missing beats is necessary since continuity of the measurement on a beat to beat basis is not needed.

[0055] In step 36, repolarization segments for each of the beats portion of the ECG signal $ECG(n)$ are extracted by quantification system 12 after the non-normal beats are removed in step 34. More specifically, in one embodiment $ST_k(n)$ segments are extracted from the ECG signal $ECG(n)$ based on two-level criterion: the first step identifies the end of the repolarization wave where the slope (first derivative) of the terminal portion of the repolarization equal or inferior to 0.1 mV. The scanning process is going forward relatively to time. If such criterion is not met because the signal does has such characteristic then : $ST_k(n) = ECG(m)$ for:

$$m \varepsilon [R(k) + D, \beta(R(k+1) - R(k))] \quad (1)$$

By way of example only, at a 200 Hz sampling frequency (SF), D is equal to sixteen in order to have a repolarization segment beginning 100 msec after the R peak of the complex k. β is equal to 4/7 for normal range of heart rate (50-100 bpm), but can be manually adjusted for heart rate outside of this range. As previously described, the repolarization interval is defined either by a flat segment at the end of the repolarization segment or as a portion of the RR interval

of the currently analyzed beat. All $ST_k(n)$ intervals beginning D/SF (sixteen samples at 200 Hz for 80 msec) after the R peak.

[0056] In another embodiment, $ST_k(n)$ segments are extracted from the ECG signal $ECG(n)$ from a starting time S_0 for each segment until an endpoint of the T wave is reached at T_o for each segment. The starting time S_0 for each segment is established as a first period of time, such as 100 msec after the R peak, although this time can vary as needed. For example, the particular point for starting time S_0 can be modified in order to avoid including QRS complex components in the area based measurements when a patient has electrical abnormalities leading to an increased QRS complex duration, such as patient with bundle branch block. In this embodiment, the starting time S_0 is set by an operator after analyzing the ECG signal for a particular subject, although the starting time S_0 could be established in other manners, such as by an analysis of a characteristic or characteristics of the ECG signal by the quantification system 12. In this embodiment, the endpoint of the T wave T_o for each segment is established when the slope of the T wave goes below a threshold slope which is set in the quantification system 12, although the endpoint of the T wave can be established in other manners. This threshold slope can be changed by the operator. The slope of the T wave portion of the segment is taken by the quantification system 12 by taking a derivative of the T wave portion of that segment, although the quantification system can determine the slope in other manners.

[0057] In this embodiment, a median signal $ST_r(n)$ is computed from a set of segments $ST_k(n)$ such as: $ST_r(n)$= median([ST_3(n), ..., ST_{NB-2}(n)]). The index r identifies the set of NB beats, with the values of r ranging from three to NB-2. For instance, as described earlier the initial portion of the ECG(n) can include seventy beats with two beats removed at each of the extremities of the portion of the ECG signal resulting in sixty-six beats analyzed with each analyzed set being eleven beats, although the size of the analyzed set can vary as needed.

[0058] In step 38, in one embodiment an area based repolarization interval for each of the extracted repolarization segments $ST_k(n)$ for the portion of the ECG signal $ECG(n)$ are obtained or measured by the quantification system 12. The area is obtained by the mathematical integration of each of the extracted repolarization segments $ST_k(n)$ by the quantification system 12 from the starting time S_0 to various percentages of the ST segment $ST_k(n)$. The time needed to reach different percentages of the total area from the starting time S_0 (shown in FIG. 3B) is measured and recorded. In this particular embodiment, the times needed to reach 25%, 50%, 90% and 97% of the area based repolarization interval for each of the extracted repolarization segment $ST_k(n)$ are recorded, although other percentages can be used. If median signal $ST_r(n)$ are computed, then the area based repolarization intervals are based on median signal $ST_r(n)$, instead of on the individual segments $ST_k(n)$. By way of example, six area based repolarization intervals are superimposed as shown in FIG. 6A and their cumulative repolarization curves are shown in FIG. 6B.

[0059] In step 40, the quantification system 12 determines if there are any more ECG signals to process. If there are more ECG signals to process, then the Yes branch is taken back to step 30. If there are no more ECG signals to process, then the No branch is taken back to step 42.

[0060] In step 42, the quantified area based repolarization interval or intervals are calculated. The calculated interval or intervals may be output or displayed in a variety of different formats, such as on an hourly basis, a day/night basis, or on a twenty-four hour basis.

[0061] The quantified area based repolarization interval or intervals may also be analyzed by quantification system 12 to detect any alterations in ventricular repolarization. In this particular embodiment, the morphology of the ventricular repolarization segment is analyzed by looking at the length of the interval needed to reach a certain percentage of A(n). For example, if the time need to reach a certain percentage deviates from a designated standard by more

than a standard deviation, then the ventricular repolarization is designated as altered.

[0062] The quantified area based repolarization intervals allow for the identification of slow trends in the area based repolarization interval. For example, in the study of pharmacological agents, the morphology of the area based repolarization interval before, during and/or after exposure to the pharmacological agent can be examined to identify trends and problems.

[0063] Quantification system 12 may perform other types of analysis, such as repolarization duration vs. cycle length relationship - paired RTx% and RR intervals are determined, the RTx%/RR) slope and its 95% confidence interval are obtained and the scattergram of the raw RTx% vs. RR relationship is graphically displayed. The slope of the regression line is a measure of QT dynamicity.

[0064] Quantification system 12 may compare RTx% by RR interval bins to determine if there has been a change in the RTx% interval with an intervention that also may have a small effect on the heart rate, the RTx% interval is grouped into selected RR interval ranges, thus avoiding the need to correct for heart rate. One example of this approach is shown in the table in FIG. 7. In this table in FIG. 7, RTx%b refers to the RT interval during the baseline ECG recording and RTx%d refers to the RT value after drug administration. A statistical comparison of the difference between the RTx%b and RTx%d for values in the RR interval bin, such as the 601 to 700 msec RR interval range is represented by the P-value . Similar comparisons are provided for other RR interval bins, such as 701-800 msec and 801-900 msec as shown in FIG. 7, with RTx% values represented by X1 to X4. RR interval bins can be arbitrarily selected by the operator of the quantification system 12.

[0065] Referring to FIGS. 8A-24B, the output form the analysis of one patient with the present invention is illustrated. Referring back to FIG. 4, this embodiment of the method ends in step 44.

[0066] The present invention described above uses the principle of signal integration of the ventricular repolarization segment to accurately identify ventricular repolarization changes induced by physiologic conditions, such as exercise, cardiac disorders, such as heart disease, or pharmacological agents, such as the evaluation of the effect of a drug on the ventricular repolarization of the heart. The present invention can be applied to ECG signals acquired in variety of dynamic settings including: short- and long-term Holter monitoring, exercise ECG testing, bedside telemetry ECG monitoring, ECG recording using event recorders, implantable devices, or intracardiac electrodes.

[0067] Having thus described the basic concept of the 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. Various alterations, improvements, and modifications will occur and are intended to those skilled in the art, though not expressly stated herein. These alterations, improvements, and modifications are intended to be suggested hereby, and are within the spirit and scope of the invention. Additionally, the recited order of processing elements or sequences, or the use of numbers, letters, or other designations therefor, is not intended to limit the claimed processes to any order except as may be specified in the claims. Accordingly, the invention is limited only by the following claims and equivalents thereto.

CLAIMS

What is claimed is:

1. A method for analyzing an electrocardiogram signal, the method comprising:

obtaining a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal; and

detecting an altered ventricular repolarization based on the obtained measured area based repolarization interval.

2. The method as set forth in claim 1 further comprising preprocessing the electrocardiogram signal, the preprocessing including at least one of:

filtering the electrocardiogram signal;

extracting a portion of the electrocardiogram signal with at least the beat; and

substantially removing any baseline from the portion electrocardiogram signal.

3. The method as set forth in claim 2 wherein the preprocessing comprises the filtering, the extracting and the substantially removing.

4. The method as set forth in claim 2 wherein the filtering further comprises:

filtering the electrocardiogram signal with a low-pass filter;

reversing the filtered electrocardiogram signal; and

filtering the reversed filtered electrocardiogram signal with the low-pass filter.

5. The method as set forth in claim 2 wherein substantially removing any baseline comprises:

estimating the baseline using a cubic spline interpolation technique; and

substantially removing the estimated baseline.

6. The method as set forth in claim 1 wherein the obtaining further comprises:

determining a starting point of a T wave in the beat in the electrocardiogram signal; and

determining an end point of the T wave in the beat in the electrocardiogram signal, wherein the portion of the electrocardiogram signal which is measured is from the starting point to the end point of the T wave.

7. The method as set forth in claim 6 wherein the starting point of the T wave is a first time after an R peak in the beat in the electrocardiogram signal.

8. The method as set forth in claim 6 wherein the end point of the T wave is when a slope of the T wave in the beat in the electrocardiogram signal goes below a first threshold.

9. The method as set forth in claim 1 wherein the obtaining further comprises:

obtaining a plurality of measurements, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a median measurement for each of the sets, wherein the detecting an altered ventricular repolarization is based on the median measurement for one or more of the sets.

10. The method as set forth in claim 9 wherein the detecting an altered ventricular repolarization further comprises:

determining a time need to reach at least a first set percentage less than one hundred percent of the median measurement for at least one of the sets; and

comparing the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected if the determined time deviates from the another time by more than a first set amount.

11. The method according to claim 10 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

12. The method according to claim 9 further comprising removing one or more of the beats which are not normal from the electrocardiogram signal.

13. The method as set forth in claim 9 further comprising removing one or more of the beats from at least one end of the electrocardiogram signal.

14. The method as set forth in claim 1 wherein the detecting an altered ventricular repolarization further comprises:

determining a time need to reach at least a first set percentage less than one hundred percent of the obtained measured area based repolarization interval; and

comparing the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected if the determined time deviates from the standard time by more than a first set amount.

15. The method according to claim 14 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

16. A computer readable medium having stored thereon instructions for analyzing an electrocardiogram signal which when executed by a processor, causes the processor to perform the steps of:

obtaining a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal; and

detecting an altered ventricular repolarization based on the obtained measured area based repolarization interval.

17. The medium as set forth in claim 15 further comprising preprocessing the electrocardiogram signal, the preprocessing including at least one of:

filtering the electrocardiogram signal;

extracting a portion of the electrocardiogram signal with at least the beat; and

substantially removing any baseline from the portion electrocardiogram signal.

18. The medium as set forth in claim 17 wherein the preprocessing comprises the filtering, the extracting and the substantially removing.

19. The medium as set forth in claim 17 wherein the filtering further comprises:

filtering the electrocardiogram signal with a low-pass filter;

reversing the filtered electrocardiogram signal; and

filtering the reversed filtered electrocardiogram signal with the low-pass filter.

20. The medium as set forth in claim 17 wherein substantially removing any baseline comprises:

estimating the baseline using a cubic spline interpolation technique; and

substantially removing the estimated baseline.

21. The medium as set forth in claim 16 wherein the obtaining further comprises:

determining a starting point of a T wave in the beat in the electrocardiogram signal; and

determining an end point of the T wave in the beat in the electrocardiogram signal, wherein the portion of the electrocardiogram signal which is measured is from the starting point to the end point of the T wave.

22. The medium as set forth in claim 21 wherein the starting point of the T wave is a first time after an R peak in the beat in the electrocardiogram signal.

23. The medium as set forth in claim 21 wherein the end point of the T wave is when a slope of the T wave in the beat in the electrocardiogram signal goes below a first threshold.

24. The medium as set forth in claim 16 wherein the obtaining further comprises:

obtaining a plurality of measurements, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a median measurement for each of the sets, wherein the detecting an altered ventricular repolarization is based on the median measurement for one or more of the sets.

25. The medium as set forth in claim 24 wherein the detecting an altered ventricular repolarization further comprises:

determining a time need to reach at least a first set percentage less than one hundred percent of the median measurement for at least one of the sets; and

comparing the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected if the determined time deviates from the standard time by more than a first set amount.

26. The medium according to claim 25 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

27. The medium according to claim 24 further comprising removing one or more of the beats which are not normal from the electrocardiogram signal.

28. The medium as set forth in claim 24 further comprising removing one or more of the beats from at least one end of the electrocardiogram signal.

29. The medium as set forth in claim 16 wherein the detecting an altered ventricular repolarization further comprises:

determining a time need to reach at least a first set percentage less than one hundred percent of the obtained measured area based repolarization interval; and

comparing the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected if the determined time deviates from the standard time by more than a first set amount.

30. The medium according to claim 29 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

31. A system for analyzing an electrocardiogram signal, the system comprising:

a measurement system that obtains a measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal; and

a detection system that detects an altered ventricular repolarization based on the obtained measured area based repolarization interval.

32. The system as set forth in claim 31 further comprising a preprocessing system that includes at least one of:

a filter system that filters the electrocardiogram signal;

an extraction system that extracts a portion of the electrocardiogram signal with at least the beat; and

a baseline removal system that substantially removes any baseline from the portion electrocardiogram signal.

33. The system as set forth in claim 32 wherein the preprocessing system comprises the filter system, the extraction system and the baseline removal system.

34. The system as set forth in claim 32 wherein the filter system further comprises a bi-directional, low pass filter that filters the electrocardiogram signal.

35. The system as set forth in claim 32 wherein baseline removal system further comprises an estimation system that estimates the baseline using a cubic spline interpolation technique, the baseline removal system substantially removing the estimated baseline.

36. The system as set forth in claim 32 wherein the measurement system further comprises a determining system that determines a starting point of a T wave in the beat in the electrocardiogram signal and an end point of the T wave in the beat in the electrocardiogram signal, wherein the portion of the electrocardiogram signal which is measured is from the starting point to the end point of the T wave.

37. The system as set forth in claim 36 wherein the starting point of the T wave is a first time after an R peak in the beat in the electrocardiogram signal.

38. The system as set forth in claim 36 wherein the end point of the T wave is when a slope of the T wave in the beat in the electrocardiogram signal goes below a first threshold.

39. The system as set forth in claim 31 wherein the measurement system further comprises a median measurement determining system that obtains a plurality of measurements, wherein each of the measurements is of a different beat in the electrocardiogram signal, divides the obtained plurality of measurements into one or more sets, and determines a median measurement for each of the sets, wherein the detecting an altered ventricular repolarization is based on the median measurement for at least one of the sets.

40. The system as set forth in claim 39 wherein the detection system further comprises:

a determining system that determines a time need to reach at least a first set percentage less than one hundred percent of the median measurement for one or more of the sets; and

a comparison system that compares the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected by the detection system if the determined time deviates from the another time by more than a first set amount.

41. The system according to claim 40 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

42. The system according to claim 39 further comprising a removal system that removes one or more of the beats which are not normal from the electrocardiogram signal.

43. The system as set forth in claim 39 further comprising a removing system that removes one or more of the beats from at least one end of the electrocardiogram signal.

44. The system as set forth in claim 31 wherein the detection system further comprises:

a determining system that determines a time need to reach at least a first set percentage less than one hundred percent of the obtained measured area based repolarization interval; and

a comparison system that compares the determined time need to reach the first set percentage against another time to reach the first set percentage, wherein an altered ventricular repolarization is detected by the detection system if the determined time deviates from the another time by more than a first set amount.

45. The system according to claim 44 wherein the another time comprises at least one of a standard time and another determined time to reach the first set percentage.

46. A method for analyzing an effect of a pharmacological agent on an electrocardiogram signal, the method comprising:

obtaining a first measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal;

administering the pharmacological agent;

obtaining a second measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal from at least one of a first period during which the pharmacological agent is in effect and a second period after the pharmacological agent is no longer in effect; and

detecting an altered ventricular repolarization based on the first and second measurements.

47. The method as set forth in claim 46 wherein the obtaining a first measurement further comprises:

obtaining a plurality of measurements from beats in the electrocardiogram signal before the administering of the pharmacological agent, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a first median measurement for each of the sets, wherein the first measurement is the first median measurement for at least one of the sets.

48. The method as set forth in claim 46 wherein the obtaining a second measurement further comprises:

obtaining a plurality of measurements from beats in the electrocardiogram signal from at least one of the first period during which the pharmacological agent is in effect and the second period after the pharmacological agent is no longer in effect, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a second median measurement for each of the sets, wherein the second measurement is the second median measurement for at least one of the sets.

49. The method as set forth in claim 46 wherein the detecting further comprises comparing the first and second measurements and determining a difference between the first and second measurements, the detecting an altered ventricular repolarization is based on the determined difference.

50. The method as set forth in claim 46 wherein the detectiing further comprises:

determining a first time need to reach at least a first set percentage less than one hundred percent of the first obtained measured area based repolarization interval;

determining a second time need to reach at least the first set percentage of the second obtained measured area based repolarization interval; and

comparing the determined first time against the determined second time to determine a difference, wherein an altered ventricular repolarization is detected based on the determined difference.

51. A computer readable medium having stored thereon instructions for analyzing an effect of a pharmacological agent on an electrocardiogram signal which when executed by a processor, causes the processor to perform the steps of:

obtaining a first measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal;

administering the pharmacological agent;

obtaining a second measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal from at least one of a first period during which the pharmacological agent is in effect and a second period after the pharmacological agent is no longer in effect; and

detecting an altered ventricular repolarization based on the first and second measurements.

52. The medium as set forth in claim 51 wherein the obtaining a first measurement further comprises:

obtaining a plurality of measurements from beats in the electrocardiogram signal before the administering of the pharmacological agent, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a first median measurement for each of the sets, wherein the first measurement is the first median measurement for at least one of the sets.

53. The medium as set forth in claim 51 wherein the obtaining a second measurement further comprises:

obtaining a plurality of measurements from beats in the electrocardiogram signal from at least one of the first period during which the pharmacological agent is in effect and the second period after the pharmacological agent is no longer in effect, wherein each of the measurements is of a different beat in the electrocardiogram signal;

dividing the obtained plurality of measurements into one or more sets; and

determining a second median measurement for each of the sets, wherein the second measurement is the second median measurement for at least one of the sets.

54. The medium as set forth in claim 51 wherein the detecting further comprises comparing the first and second measurements and determining a difference between the first and second measurements, the detecting an altered ventricular repolarization is based on the determined difference.

55. The medium as set forth in claim 51 wherein the detecting further comprises:

determining a first time need to reach at least a first set percentage less than one hundred percent of the first obtained measured area based repolarization interval;

determining a second time need to reach at least the first set percentage of the second obtained measured area based repolarization interval; and

comparing the determined first time against the determined second time to determine a difference, wherein an altered ventricular repolarization is detected based on the determined difference.

56. A system for analyzing an effect of a pharmacological agent on an electrocardiogram signal, the system comprising:

a measurement system that obtains a first measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal before administering the pharmacological agent and obtains a second measurement of an area based repolarization interval from at least one beat in the electrocardiogram signal from at least one of a first period during which the pharmacological agent is in effect and a second period after the pharmacological agent is no longer in effect; and

a detection system that detects an altered ventricular repolarization based on the first and second measurements.

57. The system as set forth in claim 56 wherein the measurement system further comprises a median measurement system that obtains a plurality of measurements from beats in the electrocardiogram signal before the administering of the pharmacological agent, wherein each of the measurements is of a different beat in the electrocardiogram signal, divides the obtained plurality of measurements into one or more sets, and determines a first median measurement for each of the sets, wherein the first measurement is the first median measurement for at least one of the sets;

wherein the median measurement system obtains a plurality of measurements from beats in the electrocardiogram signal from at least one of the first period during which the pharmacological agent is in effect and the second period after the pharmacological agent is no longer in effect, wherein each of the measurements is of a different beat in the electrocardiogram signal, divides the obtained plurality of measurements into one or more sets, and determines a second median measurement for each of the sets, wherein the second measurement is the second median measurement for at least one of the sets.

58. The system as set forth in claim 56 wherein the detection system further comprises a comparison system that compares the first and second measurements and determines a difference between the first and second measurements, the detection system detects an altered ventricular repolarization is based on the determined difference.

59. The system as set forth in claim 56 wherein the detection system further comprises:

a first determining system that determines a first time need to reach at least a first set percentage less than one hundred percent of the first obtained measured area based repolarization interval;

a second determining system that determines a second time need to reach at least the first set percentage of the second obtained measured area based repolarization interval; and

a comparison system that compares the determined first time against the determined second time to determine a difference, wherein an altered ventricular repolarization is detected by the detection system based on the determined difference.

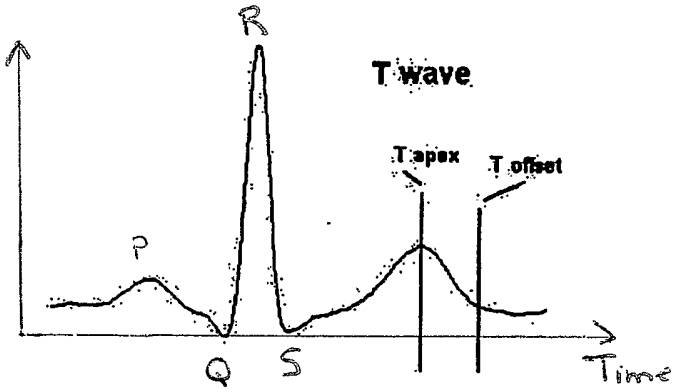
R
T wave
T apex
T offset
P
Q
S
Time

FIG. 1

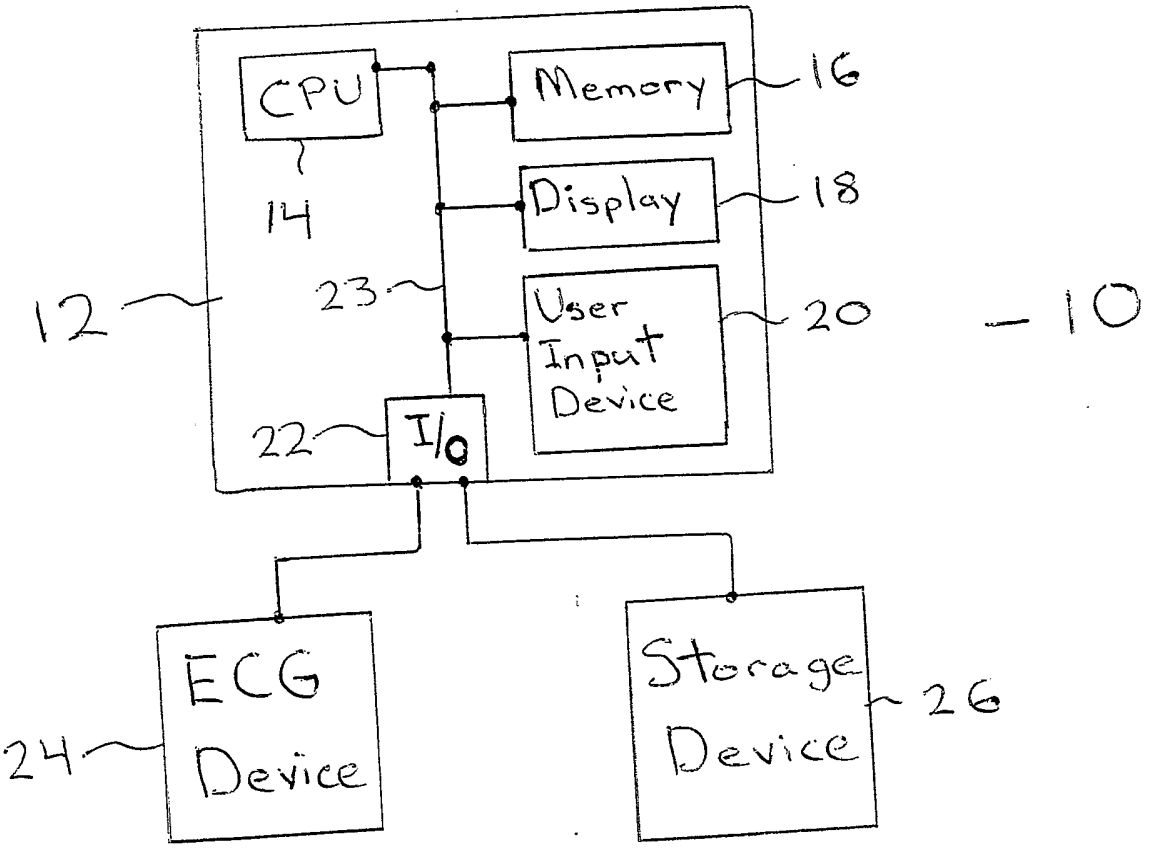
CPU
14
Memory
16
Display
18
12
23
User Input Device
20
10
22
I/O
ECG Device
24
Storage Device
26

FIG. 2

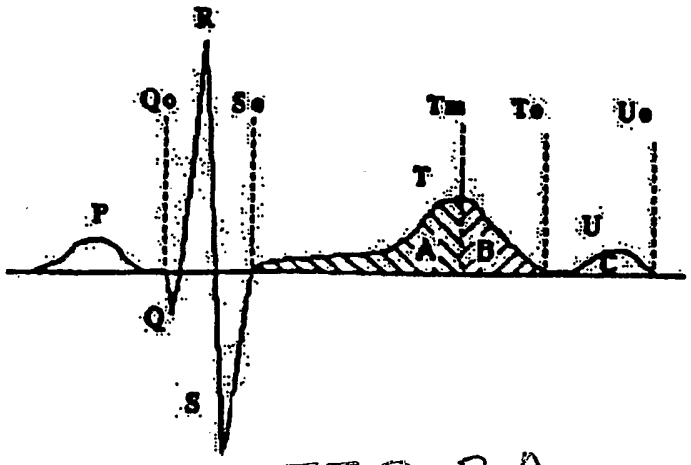
R
Qo
So
Tm
To
Uo
T
P
U
A
B
C
Q
S

FIG. 3A

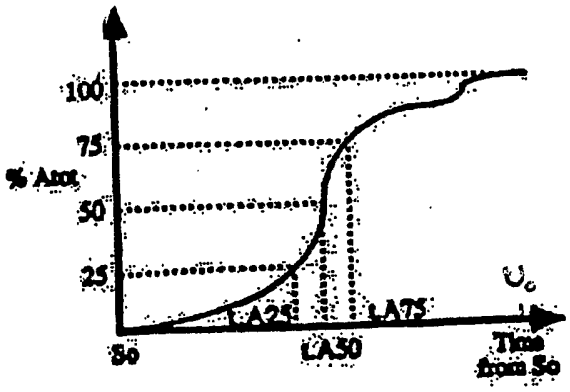
100
75
% Amt
50
25
Uo
A25
LA75
LA50
So
Time
from So

FIG. 3B

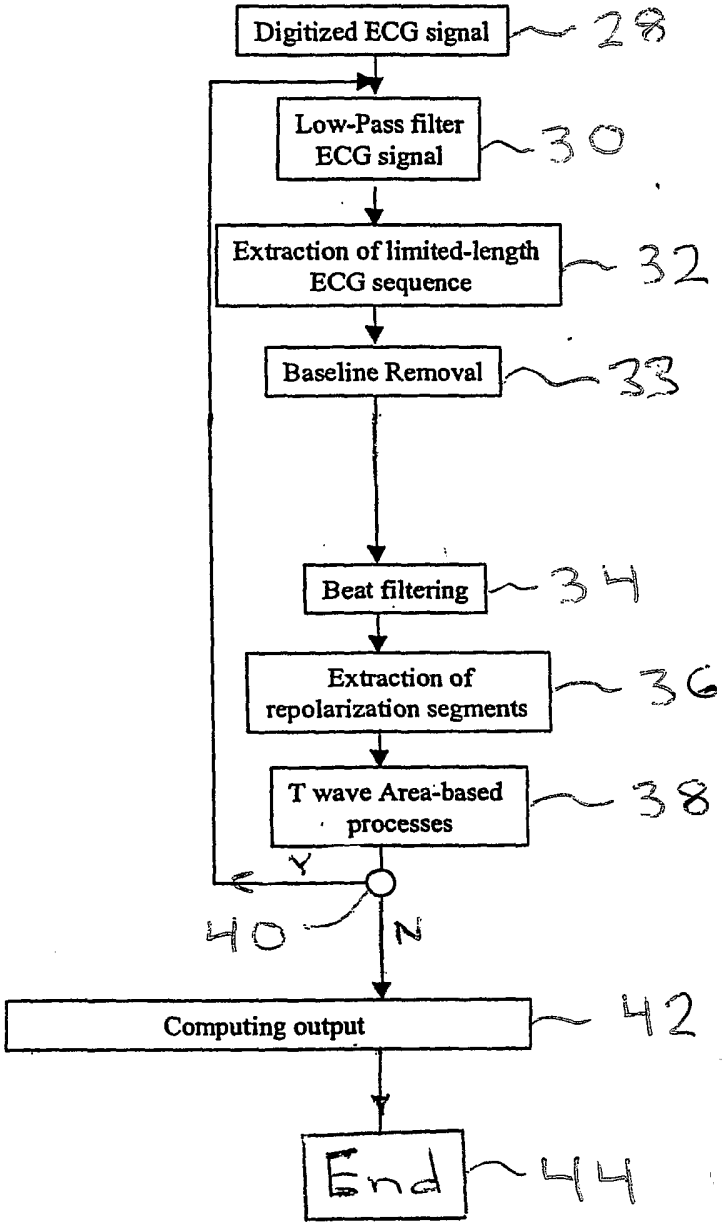
Digitized ECG signal
28
Low-Pass filter ECG signal
30
Extraction of limited-length ECG sequence
32
Baseline Removal
33
Beat filtering
34
Extraction of repolarization segments
36
T wave Area-based processes
38
Y
40
N
Computing output
42
End
44

FIG. 4

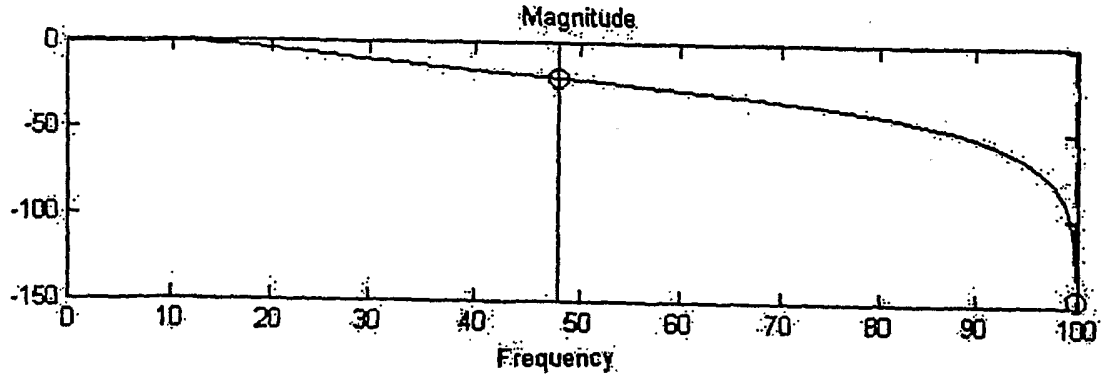

FIG. 5A

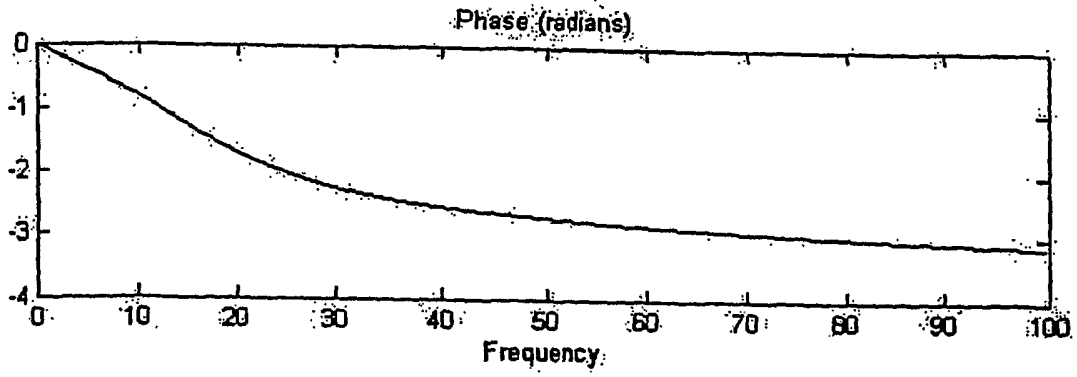

FIG. 5B

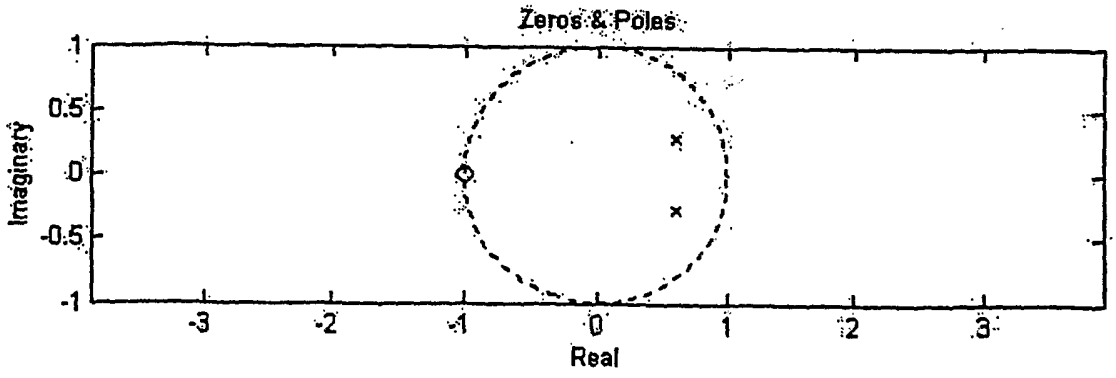

FIG. 5C

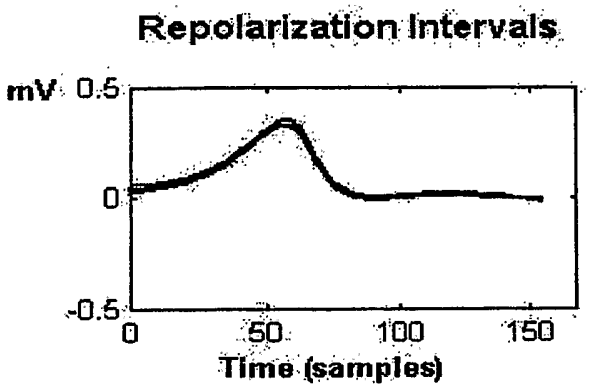
Repolarization Intervals
mV
0.5
0
-0.5
0
50
100
150
Time (samples)

FIG. 6A

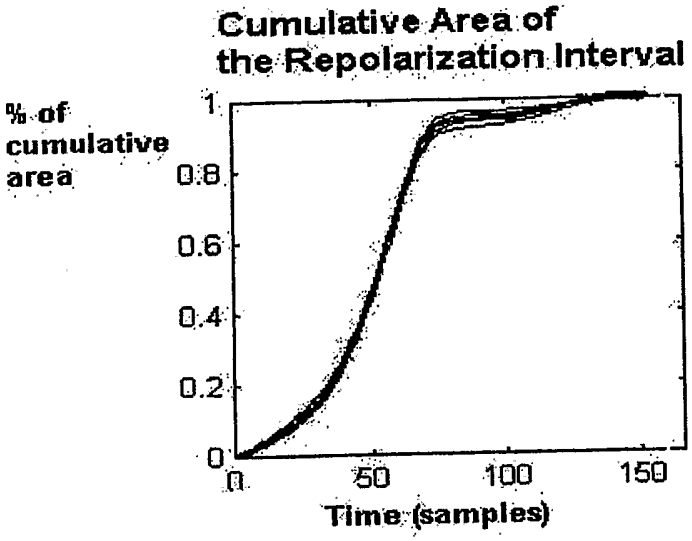
Cumulative Area of
the Repolarization Interval
% of
cumulative
area
1
0.8
0.6
0.4
0.2
0
0
50
100
150
Time (samples)

FIG. 6B

RTx% & RR Interval Bins*

	RR Interval Bins (msec)			
...	601-700	701-800	801-900	...
Baseline:	RTx%b±sd	X1	X2	
Drug:	RTx%d±sd	X3	X4	
P-value:	0.nn	0.nn	0.nn	

* avoids errors in RTx% correction for heart rate

FIG. 7

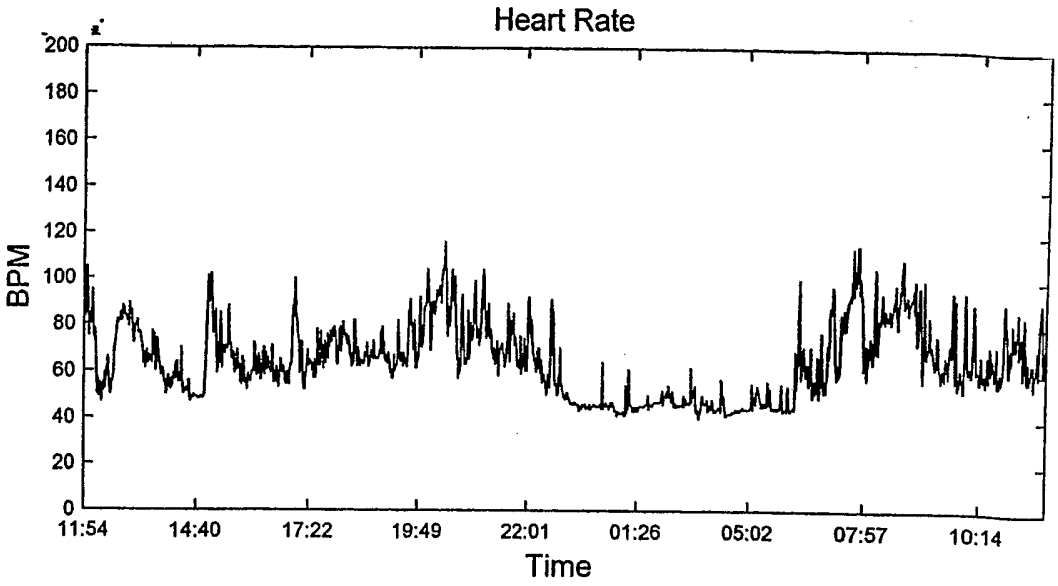
Heart Rate
BPM
200
180
160
140
120
100
80
60
40
20
0
11:54
14:40
17:22
19:49
22:01
01:26
05:02
07:57
10:14
Time

FIG. 8A

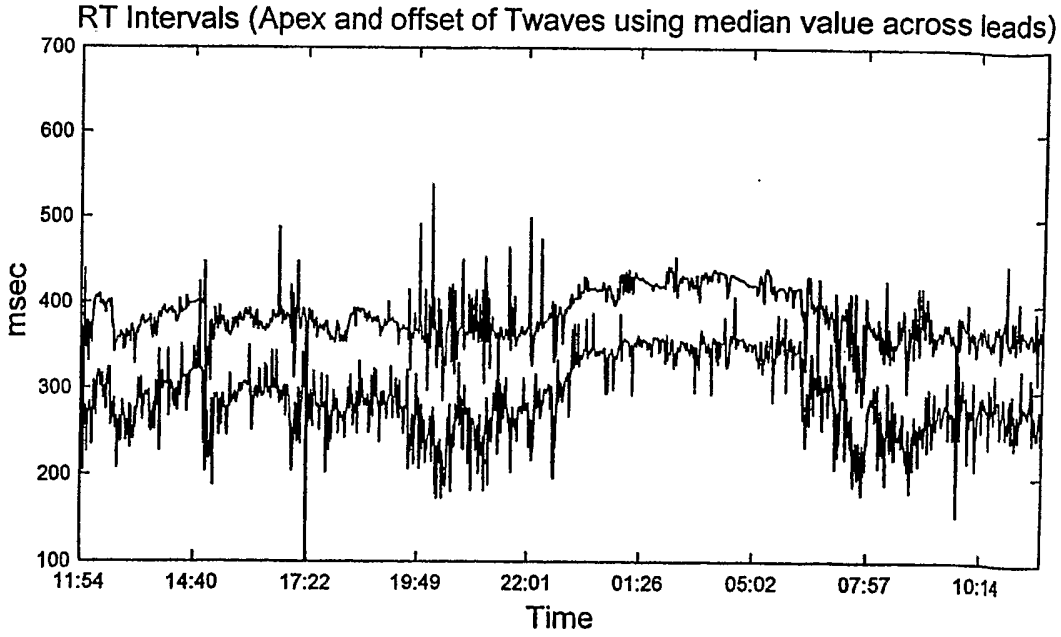
RT Intervals (Apex and offset of Twaves using median value across leads)
msec
700
600
500
400
300
200
100
11:54
14:40
17:22
19:49
22:01
01:26
05:02
07:57
10:14
Time

FIG. 8B

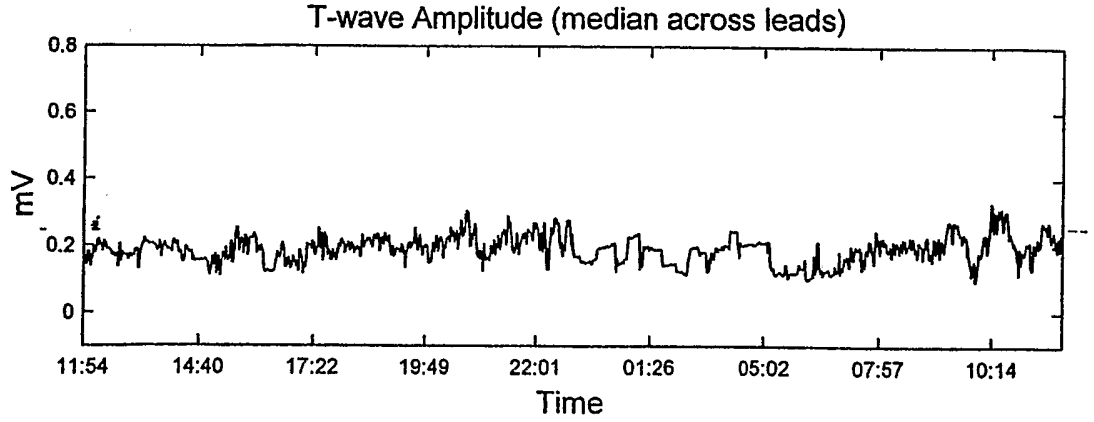

FIG. 9A

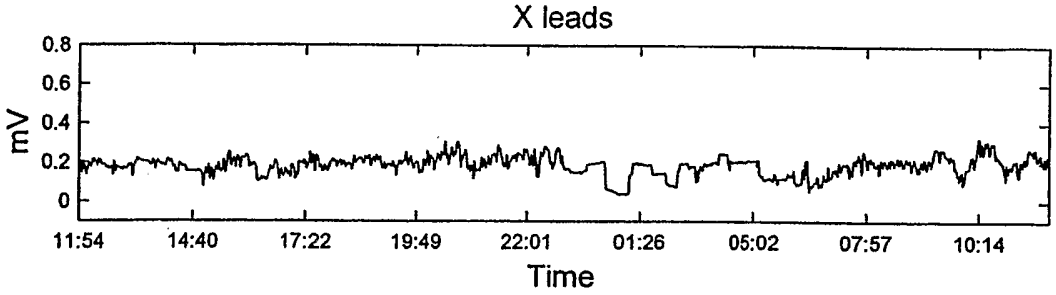

FIG. 9B

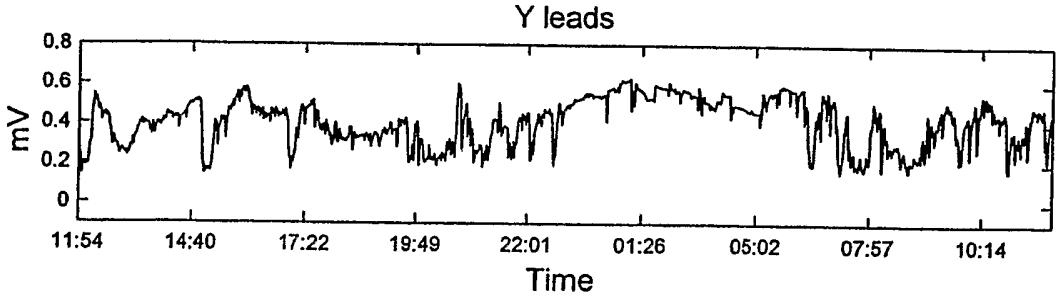

FIG. 9C

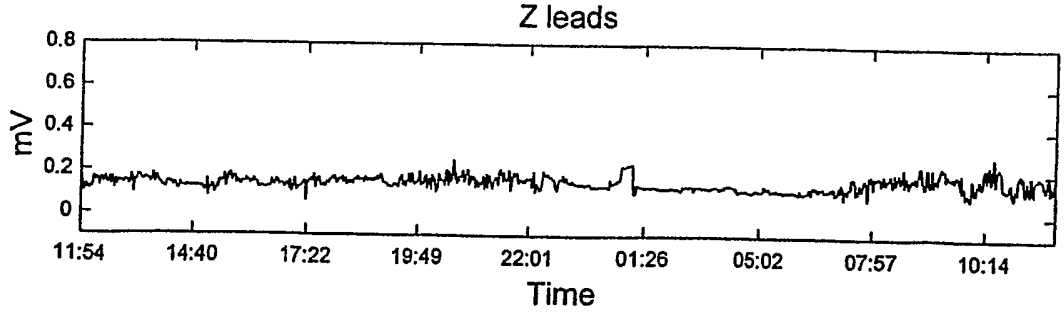

FIG. 9D

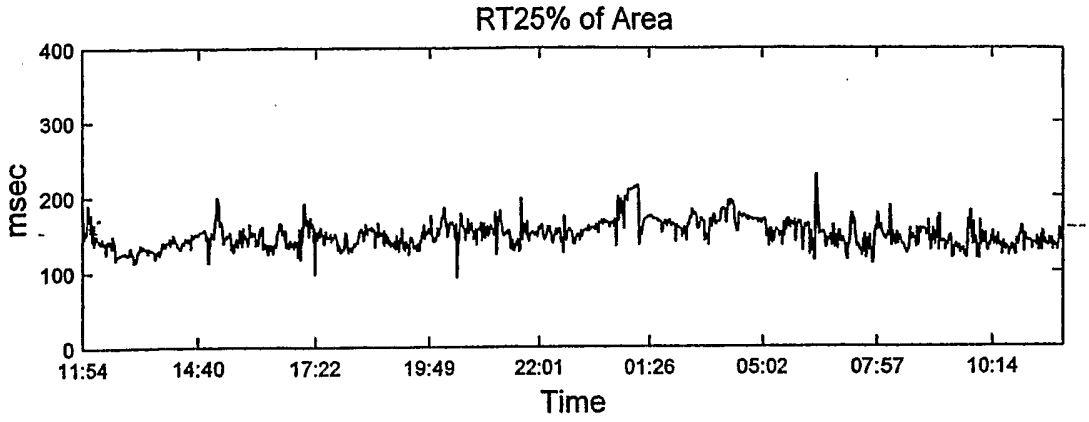

FIG. 10A

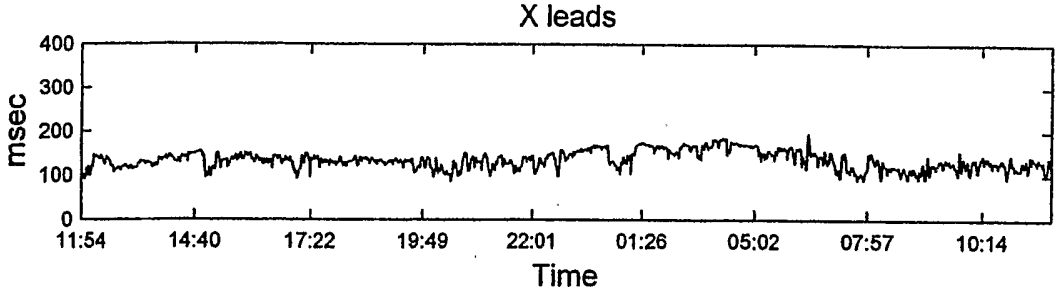

FIG. 10B

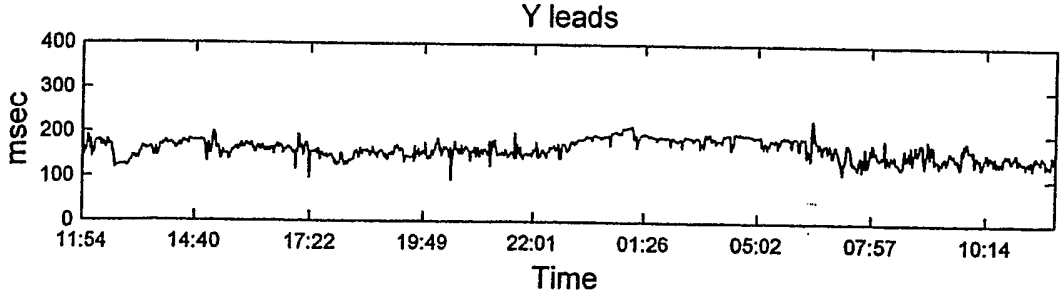

FIG. 10C

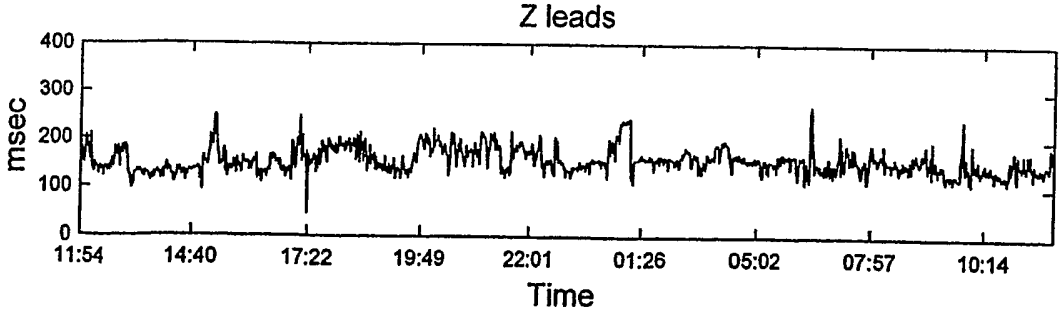

FIG. 10D

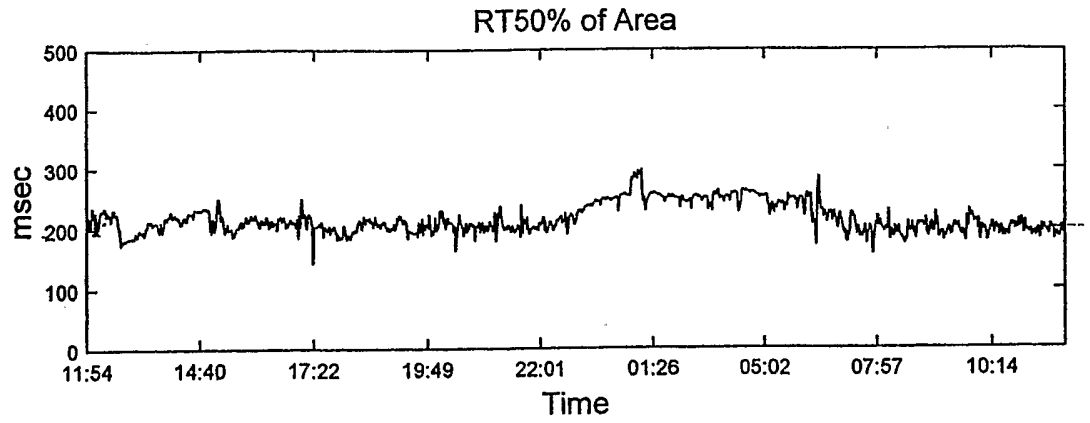

FIG. 11A

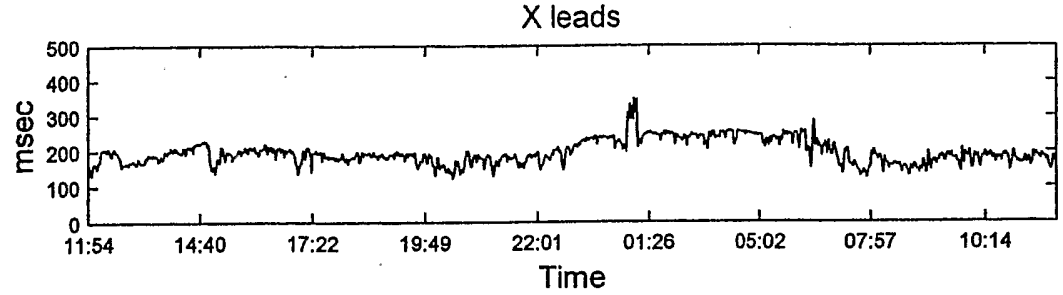

FIG. 11B

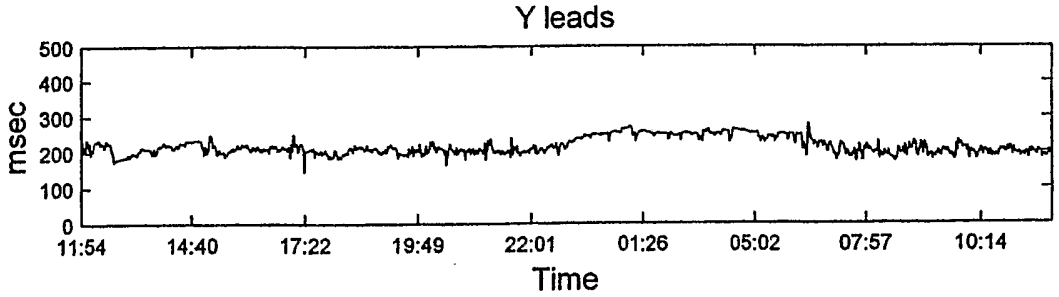

FIG. 11C

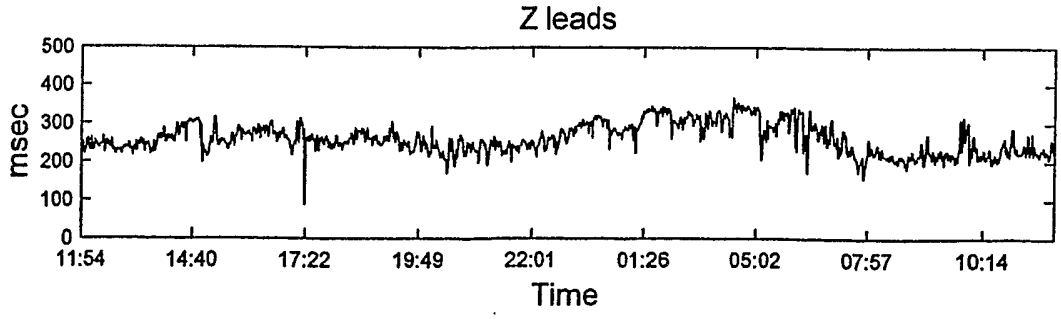

FIG. 11D

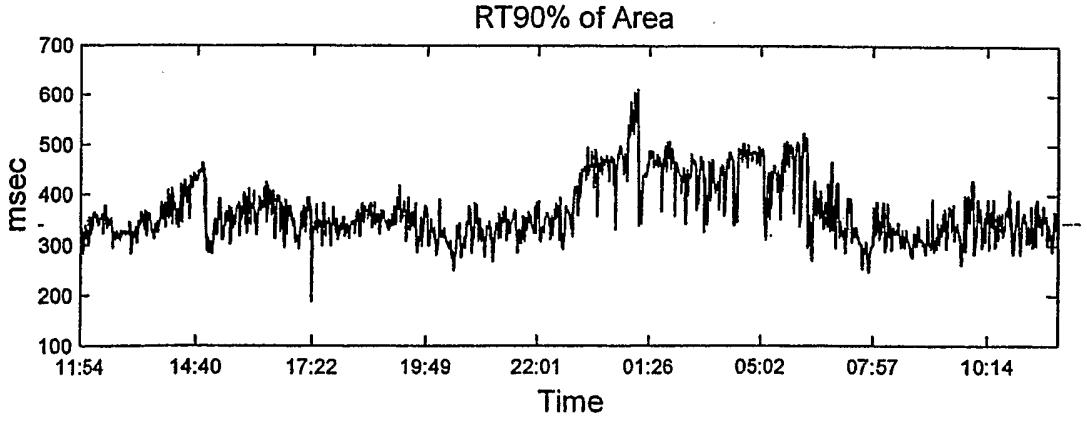

FIG. 12A

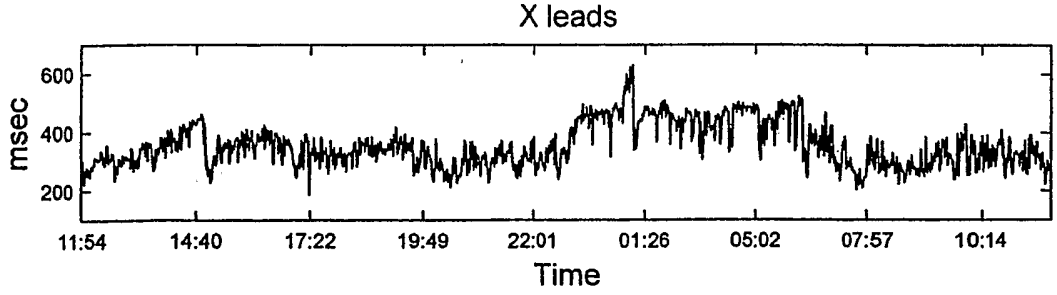

FIG. 12B

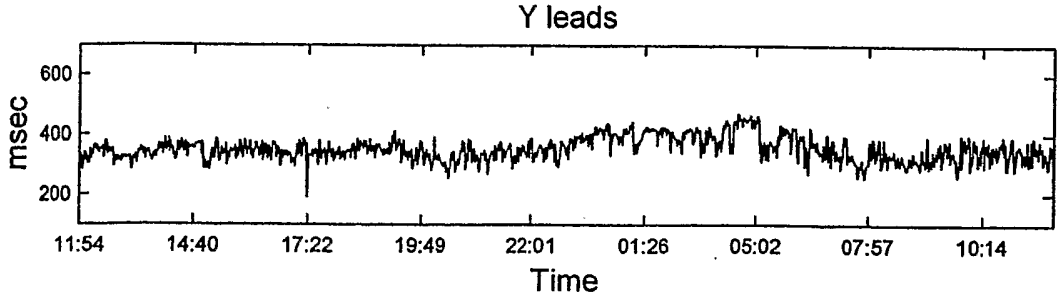

FIG. 12C

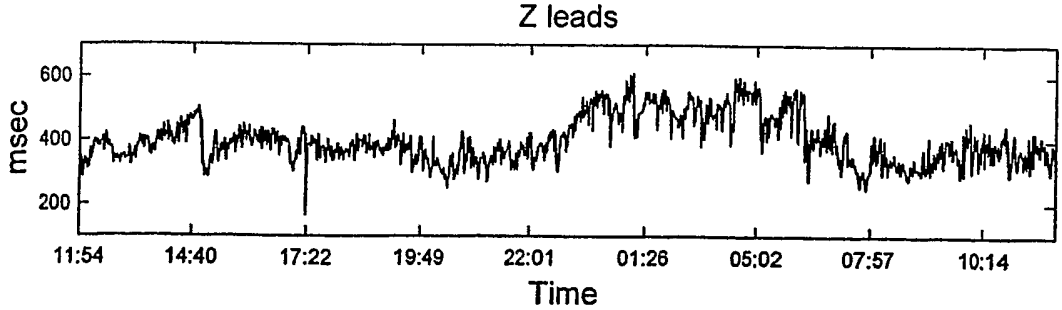

FIG. 12D

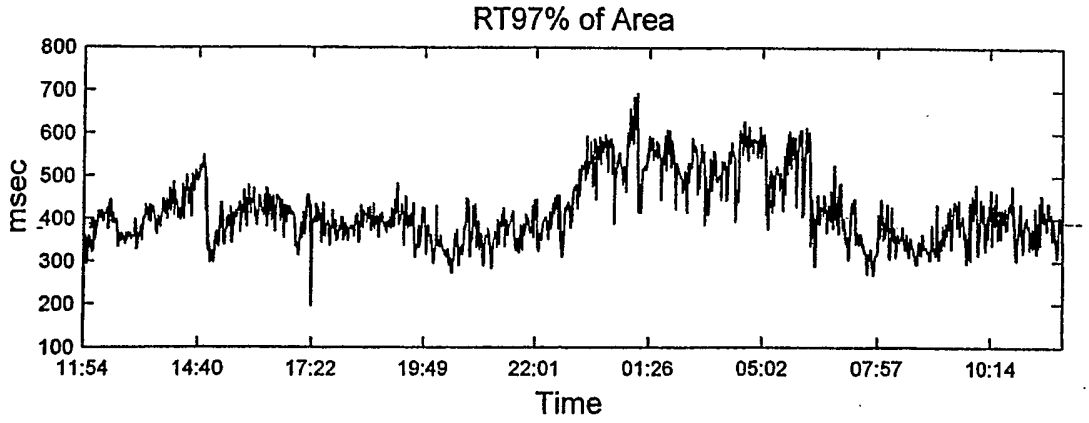

FIG. 13A

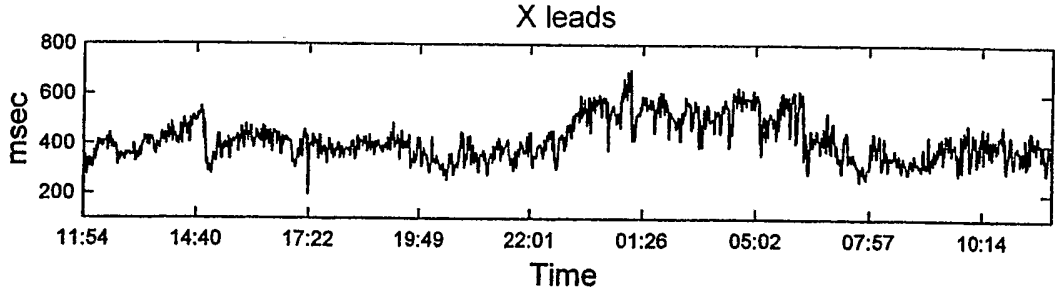

FIG. 13B

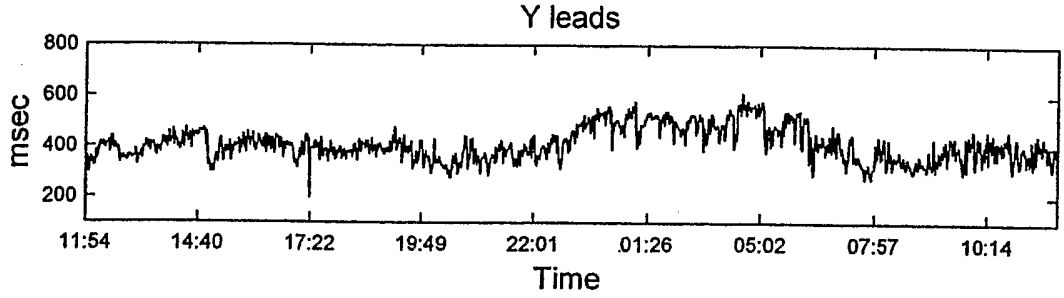

FIG. 13C

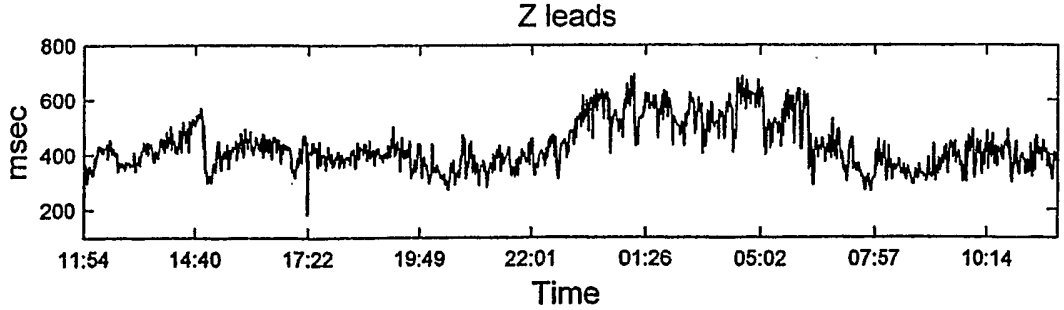

FIG. 13D

General Table (1017.twe)

	Average during 24 hours	Average during Day	Average during Night	
RR (bpm)	99	108	91	
X amplitude (mV)	0.10982	0.10078	0.11886	
Y amplitude (mV)	0.27778	0.21893	0.32782	
Z amplitude (mV)	0.14496	0.12601	0.17023	
X RT apex (msec)	235	231	240	
Y RT apex (msec)	221	207	237	
Z RT apex (msec)	217	203	232	
X RT offset (msec)	329	322	336	
Y RT offset (msec)	298	286	306	
Z RT offset (msec)	285	276	296	
X T area 25% (msec)	102	93	111	
Y T area 25% (msec)	101	93	109	
Z T area 25% (msec)	89	66	111	
X T area 50% (msec)	136	119	153	
Y T area 50% (msec)	137	121	157	
Z T area 50% (msec)	129	109	149	
X T area 90% (msec)	278	264	292	
Y T area 90% (msec)	260	246	273	
Z T area 90% (msec)	237	231	241	
X T area 97% (msec)	310	286	331	
Y T area 97% (msec)	305	282	329	
Z T area 97% (msec)	294	276	309	

FIG. 14

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	T-wave Ampl X	T-wave Ampl Y	T-wave Ampl Z
14:00	103	0.084012	0.18963	0.1001
16:00	122	0.095323	0.20489	0.12509
18:00	98	0.099484	0.21387	0.11923
20:00	99	0.10036	0.22249	0.12163
22:00	101	0.099274	0.23153	0.12482
00:00	89	0.1019	0.23955	0.12684
02:00	86	0.10516	0.25072	0.1311
04:00	76	0.10772	0.2616	0.13614
06:00	77	0.11012	0.27523	0.14485
08:00	72	0.11192	0.29008	0.15334
10:00	110	0.11036	0.28595	0.15234
12:00	118	0.10823	0.27781	0.14987

FIG. 15

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	T-wave Apex X	T-wave Apex Y	T-wave Apex Z
13:00	97	239	221	211
14:00	103	239	219	195
15:00	115	236	206	191
16:00	122	234	201	193
17:00	101	234	201	197
18:00	98	231	206	200
19:00	97	231	207	206
20:00	99	230	209	204
21:00	99	233	211	205
22:00	101	231	213	206
23:00	116	232	214	206
00:00	89	233	216	208
01:00	94	236	215	207
02:00	86	233	218	212
03:00	89	234	216	213
04:00	76	234	221	216
05:00	82	235	220	217
06:00	77	236	223	219
07:00	78	236	225	220
08:00	72	237	226	222
09:00	84	237	225	221
10:00	110	236	224	220
11:00	100	236	223	219
12:00	118	235	221	217

FIG. 16

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	T-wave Offset Lead X	T-wave Offset Lead Y	T-wave Offset Lead Z
14:00	103	369	312	291
16:00	122	321	286	265
18:00	98	321	285	270
20:00	99	325	286	277
22:00	101	336	290	278
00:00	89	331	292	279
02:00	86	328	293	281
04:00	76	328	295	284
06:00	77	327	296	286
08:00	72	327	298	289
10:00	110	325	297	289
12:00	118	323	297	285

FIG. 17

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	ABRI RT25 Xlead	ABRI RT25 Ylead	ABRI RT25 Zlead
14:00	103	106	96	64
16:00	122	92	66	49
18:00	98	92	78	59
20:00	99	94	85	68
22:00	101	97	92	71
00:00	89	100	93	74
02:00	86	101	97	80
04:00	76	102	102	85
06:00	77	103	105	90
08:00	72	104	108	95
10:00	110	103	105	93
12:00	118	102	101	89

FIG. 18

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	ABRI RT50 Xlead	ABRI RT50 Ylead	ABRI RT50 Zlead
13:00	91	122	48	126
14:00	103	169	144	112
15:00	156	121	115	92
16:00	122	148	108	93
17:00	101	131	111	98
18:00	98	148	118	104
19:00	97	139	124	109
20:00	99	151	123	112
21:00	90	131	116	115
22:00	101	154	130	116
23:00	110	155	130	115
00:00	89	155	132	118
01:00	94	144	124	120
02:00	86	155	135	122
03:00	85	155	127	122
04:00	76	156	139	127
05:00	73	152	131	126
06:00	77	157	141	131
07:00	76	150	132	133
08:00	72	157	144	134
09:00	95	150	138	136
10:00	110	157	141	133
11:00	106	156	139	131
12:00	118	156	137	129

FIG. 19

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	ABRI RT90 Xlead	ABRI RT90 Ylead	ABRI RT90 Zlead
13:00	99	281	262	243
14:00	103	283	271	243
15:00	145	262	241	223
16:00	122	257	236	219
17:00	101	260	240	222
18:00	98	262	243	225
19:00	97	264	246	227
20:00	99	266	248	235
21:00	90	265	249	237
22:00	101	270	252	240
23:00	116	269	252	239
00:00	89	271	255	238
01:00	91	270	257	237
02:00	86	274	259	236
03:00	84	275	260	236
04:00	76	277	261	235
05:00	87	276	261	235
06:00	77	280	264	237
07:00	76	280	265	237
08:00	72	282	266	238
09:00	96	281	266	238
10:00	110	280	263	238
11:00	106	280	262	238
12:00	118	278	260	237

FIG. 20

Hourly Table (1017.twe)

Time	Heart Rate (BPM)	ABRI RT97 Xlead	ABRI RT97 Ylead	ABRI RT97 Zlead
14:00	103	306	304	297
16:00	122	275	269	264
18:00	98	283	279	274
20:00	99	288	284	280
22:00	101	292	288	285
00:00	89	294	291	285
02:00	86	299	296	288
04:00	76	305	302	291
06:00	77	311	307	295
08:00	72	315	312	299
10:00	110	313	309	297
12:00	118	310	305	294

FIG. 21

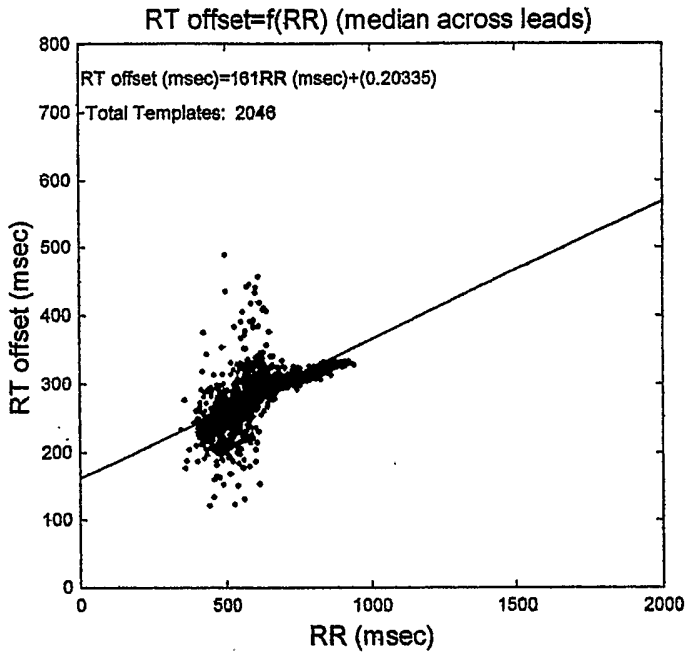

FIG. 22A

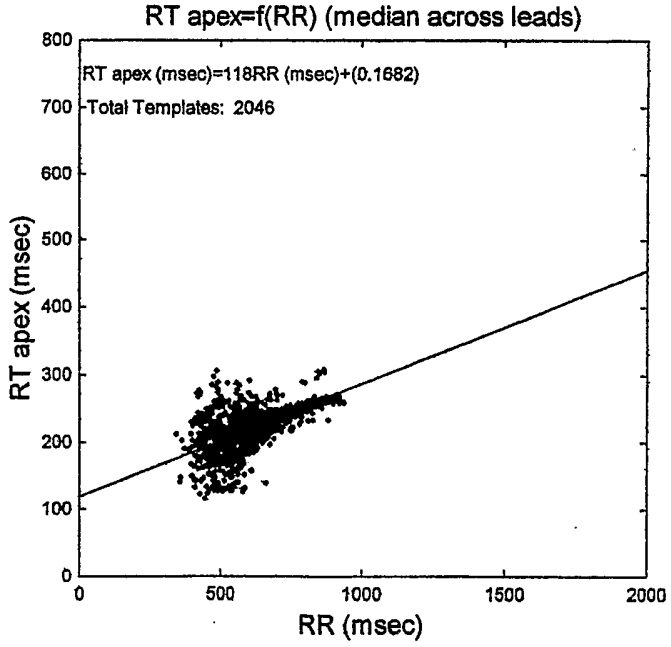

FIG. 22B

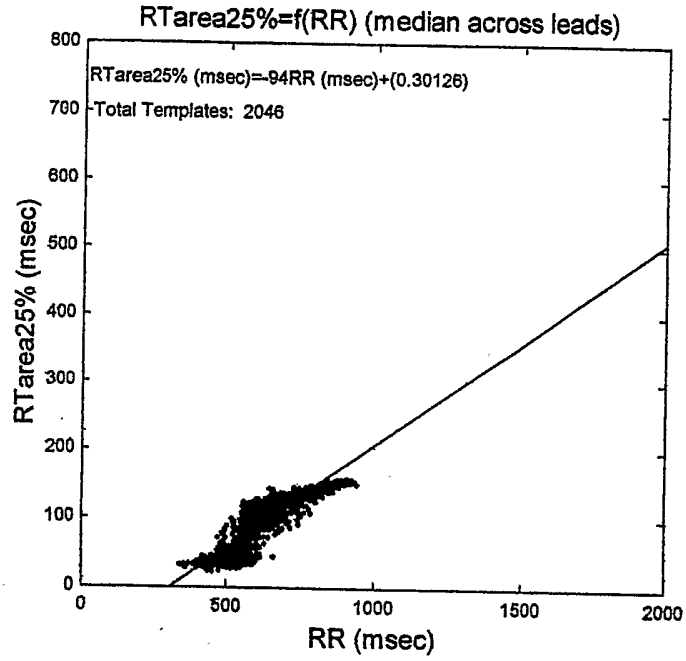

FIG. 23A

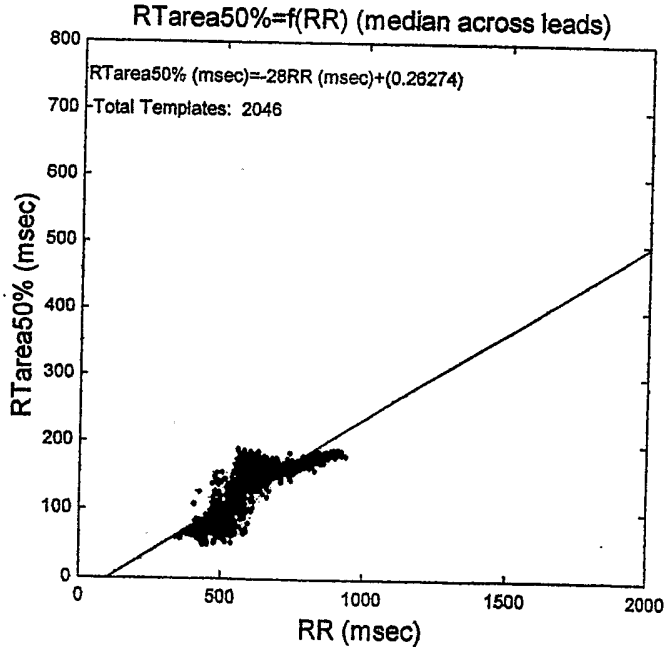

FIG. 23B

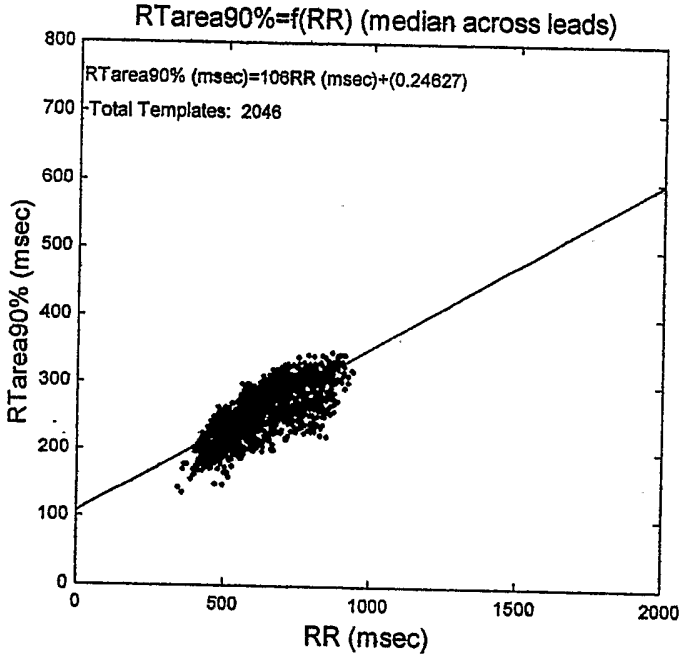

FIG. 24A

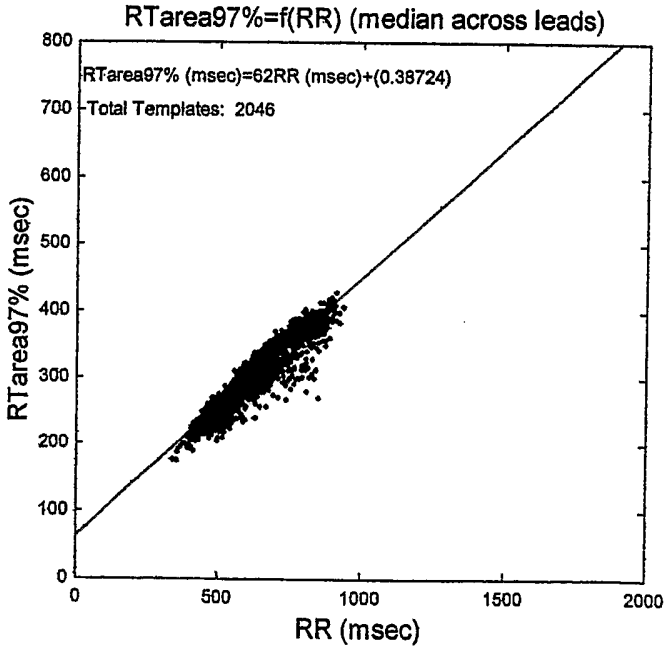

FIG. 24B