

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
5 February 2009 (05.02.2009)

PCT

(10) International Publication Number
WO 2009/018570 A2

- (51) International Patent Classification:
A61B 5/0402 (2006.01)
- (21) International Application Number:
PCT/US2008/072099
- (22) International Filing Date: 4 August 2008 (04.08.2008)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/953,508 2 August 2007 (02.08.2007) US
61/084,389 29 July 2008 (29.07.2008) US

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(71) Applicant (for all designated States except US): THE RESEARCH FOUNDATION OF STATE UNIVERSITY OF NEW YORK [US/US]; Albany, NY 12201-0009 (US).

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

- (72) Inventors; and
- (75) Inventors/Applicants (for US only): CHON, Ki [US/US]; Dept Biomedical Engrg, Stony Brook University, Stony Brook, NY 11794-3369 (US). RAEDER, Ernst [US/US]; Cardiology Division, Stony Brook University, Stony Brook, NY 11794-3369 (US).

Declaration under Rule 4.17:
— of inventorship (Rule 4.17(iv))

(74) Agent: GALLAGHER, John, F., III; The Farrell Law Firm, P.S., 333 Earle Ovington Blvd. Ste 701, Uniondale, NY 11553 (US).

Published:
— without international search report and to be republished upon receipt of that report

(54) Title: RR INTERVAL MONITORING AND BLOOD PRESSURE CULFF UTILIZING SAME

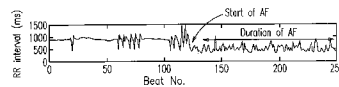


FIG. 1(a)

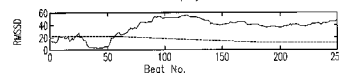


FIG. 1(b)

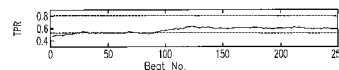


FIG. 1(c)

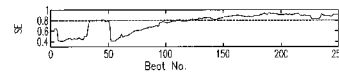


FIG. 1(d)

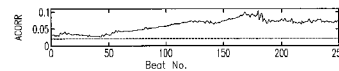


FIG. 1(e)

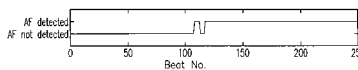


FIG. 1(f)

(57) Abstract: Disclosed is an apparatus and method for ambulatory, real-time detection of Atrial Fibrillation (AF) providing an overall accuracy that refers to detection of AF, irrespective of the duration of AF and beat-to-beat classification.

WO 2009/018570 A2

**RR INTERVAL MONITORING METHOD AND
BLOOD PRESSURE CUFF UTILIZING SAME**

PRIORITY

This application claims priority to U.S. Provisional Application No. 60/953,508,
5 filed August 2, 2007, and to U.S. Provisional Application No. 61/084,389, filed
July 29, 2008, the contents of each of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

The present invention applies an algorithm for detection of Atrial Fibrillation
(AF), which is one of the most common cardiac arrhythmias, afflicting approximately 2-3
10 million Americans. The incidence and prevalence of AF increase with age. With the
graying of the baby boomers, it is estimated that 12-16 million individuals may be
affected by 2050 and be at risk of significant mortality and morbidity from this
arrhythmia.

AF has a prevalence of 17.8% and an incidence of 20.7/1,000 patient years in
15 individuals older than 85. At age 55, the lifetime risk of developing AF is approximately
23%. AF is an independent risk factor for death (relative risk in men is 1.5 and in women
1.9). Furthermore, AF is a major cause of ischemic stroke, the impact of which increases
with age and reaches 23.5% in patients older than 80. Accurate detection of AF is crucial
since effective treatment modalities such as chronic anticoagulation and antiarrhythmic
20 therapy, as well as radiofrequency ablation, are available but carry risks of serious
complications. Despite the ubiquity of the arrhythmia, its diagnosis rests largely on the
presence of symptoms and on serendipity. Unfortunately, since patients are often
unaware of their irregular pulse, the diagnosis is often only established during a fortuitous
doctor visit. If episodes of AF occur interspersed with normal sinus rhythm, the
25 diagnosis presents an even greater challenge.

When AF is suspected, ambulatory monitoring can be performed in an attempt to
document the arrhythmia. However, this approach is time consuming and not cost-
effective for screening asymptomatic populations. Limitations of currently available
technology including electrocardiography (for less than 10 seconds) and long-term
30 monitoring. Ambulatory Holter monitoring is limited to no more than 48 hours and is
cumbersome because it requires several leads connecting to a device worn on the

patient's waist. After completion of the recording, the monitor is returned for data analysis by a cardiologist. Accordingly, real-time monitoring is not possible with conventional devices.

Conventional monitoring devices also include event monitors, which are small devices carried by a patient for up to 30 days. The patient will activate the event monitor upon when experiencing an irregular heart beat. A cardiologist will subsequently analyze recordings obtained by the event monitor.

For patients with very infrequent but potentially serious rhythm disturbances, an implantable loop recorder can be used. The implantable loop recorder continually records and overwrites the electrocardiogram for more than one year. When patients experience an event, they can freeze the recording and transmit the information to a cardiologist.

Several companies presently offer ambulatory heart monitors without AF detection capability. For example, CardioNet (www.cardionet.com) provides a 3-lead ECG monitor system which records and transmits data wirelessly to a hand held PDA for subsequent modem or Internet transmission. See, Rothman, et al., *Diagnosis of Cardiac Arrhythmias* Journal of Cardiovascular Electrophysiology, Vol. 18, No. 3, March 2007, U.S. Patent No. 7,212,850 and Patent Appl. Pub No. US 2006/0084881 A1 of Korzinov et al., the contents of which are incorporated herein by reference.

Conventional systems also include wireless transmission of ECG data, as discussed in U.S. Patent No. 5,522,396, a 12-lead Holter ECG system, as discussed in U.S. Patent No. 6,690,967, and an event recorder system, as discussed in U.S. Patent No. 5,876,351, the contents of each of which are incorporated herein by reference.

An AfibAlert device, see www.afibalert.com, monitors for AF during a 45-second testing period. However, the AfibAlert device does not provide a continuous or real-time detection and monitoring of the heart, and therefore cannot alert if AF happens at any other time. In addition, the cost of the AfibAlert device is relatively high for wide acceptance by the general population. Furthermore, the 90-93% accuracy of the AfibAlert device is below the accuracy of the detection algorithm of the present invention.

A number of algorithms have been developed to detect AF. Such conventional algorithms can be categorized based on P-wave detection and RR interval (RRI)

variability (HRV). Since there is no uniform depolarization of the atria during AF, there is no discernible P-wave in the ECG. This fact has been utilized in detection of AF by trying to identify whether the P-wave is absent. However, in most cases the location of the P-wave fiducial point is very difficult to find. Moreover, the P-wave may be small
5 enough to be corrupted by noise that is inherent in surface measurements. The methods in the second category do not require identification of the P-wave and are based on the variability of RRI series. However, few algorithms in this category show high predictive value for clinical application. A notable exception is discussed by Duverney et al. in *High Accuracy of Automatic Detection of Atrial Fibrillation using Wavelet Transform of Heart Rate Intervals*, Pacing Clin Electrophysiol 25: 457-462, 2002, and by Tateno et al. in
10 *Automatic Detection of Atrial Fibrillation using the Coefficient of Variation and Density Histograms of RR and delta RR Intervals*, Medical & Biological Engineering & Computing 39: 664-671, 2001.

Duverney et al. use wavelet transform of the RRI time series where the sensitivity
15 and specificity was 96.1% and 92.6% for AF beats, respectively, on a European database consisting of 15 subjects. Tateno et al. compare the density histogram of a test RRI (and Δ RRI) segment with previously compiled standard density histograms of RR (and Δ RR) segments during AF using the Kolmogorov-Smirnov test, to report a sensitivity of 94.4% and specificity of 97.2% for AF beats for the MIT BIH Atrial Fibrillation database.
20 However, the accuracy of the Tateno et al. algorithm relies on the robustness of training data and that their results were based on a limited database. However, in most clinical applications, it may be difficult to obtain such large databases of training data.

In view of a general consideration of AF as being a random sequence of heart beat intervals with markedly increased beat-to-beat variability, the present invention combines
25 four statistical techniques to exploit a Root Mean Square of Successive RR interval differences to quantify variability (RMSSD), a Turning Points Ratio to test for randomness of the time series (TPR), a Shannon Entropy (SE) to characterize its complexity and a autocorrelation (ACORR) index to characterize correlation between the first two RR intervals. In contrast to the Tateno-Glass method, the algorithm of the
30 present invention does not require training data. See, Lu S, Chon KH, and Raeder E, *Automatic Real Time Detection of Atrial Fibrillation*, Heart Rhythm 4: S36, 2007.

The present invention provides a method and apparatus for utilizing an algorithm that accurately detects, in a real-time manner, the presence of AF utilizing piezoelectric or ECG signals. The present invention also provides a portable blood pressure cuff, for home monitoring.

5

SUMMARY OF THE INVENTION

The present invention provides a real-time AF analysis by obtaining a patient heartbeat; analyzing select consecutive obtained heartbeats; selecting a beat segment of RR intervals centered on that beat for each analyzed heartbeat; eliminating ectopic beats and compensatory pause associated with each ectopic beat; calculating a root mean square of successive RR differences (RMSSD) of the beat segment; and performing a first identification that the beat segment is an AF candidate by determining whether the RMSSD is greater than a RMSSD threshold.

10

In a preferred embodiment of the presenting invention, if an AF candidate identified is made, a second identification is performed of the beat segment by calculating a TPR of the segment and determining whether the TPR satisfies randomness criteria. If it is again identified as an AF candidate, a third identification of the beat segment is performed by calculating a Shannon Entropy (SE) of the segment and determining whether the SE is greater than an SE threshold.

15

BRIEF DESCRIPTION OF THE DRAWINGS

20

The above and other objects, features and advantages of certain exemplary embodiments of the present invention will be more apparent from the following detailed description taken in conjunction with the accompanying drawings, in which:

Fig. 1 is a chart showing threshold values for AF detection;

Fig. 2 depicts random numbers subjected to turning points analysis;

25

Fig. 3 shows an AF episode, including RMSSD, TPR, Shannon Entropy and ACORR;

Fig. 4 shows a piezoelectric sensor incorporated in a blood pressure cuff;

Fig. 5 provides a comparison of RR intervals obtained from a commercial ECG device and PPV values obtained utilizing the piezoelectric sensor of the present invention;

5 Figs. 6(a) and 6(b) shows an integrated wireless ECG device and wireless ECG collection of the present invention; and

Fig. 7 is a flowchart showing operation of a preferred embodiment of the present invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

10 The following detailed description of preferred embodiments of the invention will be made in reference to the accompanying drawings. In describing the invention, explanation about related functions or constructions known in the art are omitted for the sake of clearness in understanding the concept of the invention, to avoid obscuring the invention with unnecessary detail.

15 A preferred embodiment of the present invention utilizes a Turning Points Analysis (TPA) to determine whether an RR interval sequence is random, for application of the TPA nonparametric statistical test comparing each point in the time series to neighboring points.

20 Fig. 1 shows, in panel (a), an original RR interval time series from a section of file 5162 of a MIT BIH Atrial Fibrillation database. Fig. 1 also shows calculation of the RMSSD, TPR, Shannon Entropy and ACORR, in panels (b)-(e) respectively, for the same segment is shown. Panel (f) of Fig. 1 shows final detection results based on whether the above statistics cross respective thresholds, shown in dashed lines for the respective panel.

25 Panel (a) of Fig. 1 shows a long-term recording with an episode of AF embedded in normal sinus rhythm in which random behavior of AF is clearly observed. As shown in Panels (b) through 1(f) of Fig. 1, the combination of TPR, RMSSD, SE and ACORR greatly enhances the accuracy of AF detection.

30 In a computer generated random time series, the probability of an interval being surrounded by either two higher or two lower intervals ("Turning Point") is equal to 2/3. Given three random numbers a_1, a_2, a_3 where $a_1 > a_2 > a_3$, there are six combinations to generate a series. Among them, $(a_1 a_3 a_2), (a_2 a_3 a_1), (a_2 a_1 a_3)$ and $(a_3 a_1 a_2)$ include turning

points while $(a_1a_2a_3)$ and $(a_3a_2a_1)$ do not. Given a random series of length n , the expected number of turning points is $\frac{2n-4}{3}$, and the standard deviation is $\sqrt{\frac{16n-29}{90}}$.

Hence, the expected Turning Points Ratio (TPR) of a random series is provided in Equation (1):

5
$$\text{TPR} = \frac{2n-4}{3n} \pm \sqrt{\frac{16n-29}{90}} \dots\dots\dots (1)$$

Confidence limits of this ratio are defined to estimate randomness boundaries in a time series. A series with ratios below the lower 95% confidence interval exhibits periodicity (e.g. sinus rhythm) whereas TPRs above the upper 95% confidence limit approaching 1.0 are evidence of alternans where ultimately every point is a turning point (“ABABAB” pattern).

10 Figure 2 shows an analysis of one thousand (1000) random numbers subjected to turning points analysis. As expected, Panel A shows the TPR of the random number sequence is $\sim 2/3$. When increasing levels of alternans are imposed, as shown in Panels B through D of Fig. 2, the TPR increases above the 95% confidence limit for randomness until approaching unity.

15 In the present invention, a Root Mean Square of Successive Differences is preferably performed as a second component of the algorithm. In the present invention, beat-to-beat variability is estimated by the root mean square of successive RR differences (RMSSD). Since AF exhibits higher variability between adjacent RR intervals than periodic rhythms such as sinus rhythm, the RMSSD is expected to be higher. For a given segment $a(i)$ of RR intervals of some length l , the RMSSD is given by Equation (2):

$$\text{RMSSD} = \sqrt{\frac{1}{128} \sum_j^{j+l-1} (a(j+1) - a(j))^2} \dots\dots\dots (2)$$

A third component of the algorithm of the present invention is Shannon Entropy (SE), which provides quantitative information about the complexity of a signal.

25 Complexity refers to the difficulty in describing or understanding a signal. For example, signals with discernible regular patterns are easier to describe than signals with a higher degree of irregularity. The SE quantifies how likely runs of patterns that exhibit

regularity over a certain duration of data also exhibit similar regular patterns over the next incremental duration of data. For example, a random white noise signal is expected to have the highest SE value (1.0) whereas a simple sinusoidal signal will have a very low SE (~ 0.2) value. Thus, the SE values of normal sinus rhythm and AF can be expected to differ significantly.

5

Calculation of SE of the RR interval time series is performed by first constructing a histogram of the segment considered. The eight maximum and eight minimum RR values in the segment are considered outliers and are removed from consideration. The remaining RR intervals are sorted into equally spaced bins whose limits are defined by the minimum and maximum RR interval after removing outliers. To obtain a reasonably accurate measure of the SE, at least 16 such bins are needed. Based on an ROC curve analysis, the segment length for AF detection was set at 128 beats.

10

An estimation of probability is performed as a next step in the calculation of SE, preferably by computing for each bin as the number of beats in that bin divided by the total number of beats in the segment (after removing outliers), for example see Equation (3):

15

$$p(i) = \frac{\text{Na of beats in bin}(i)}{\text{Total number of beats in the segment}} = \frac{\text{Na of beats in bin}(i)}{128-16} = \frac{\text{Na of beats in bin}(i)}{112} \dots\dots(3)$$

The SE is then calculated utilizing Equation (4):

20

$$SE = - \sum_{i=1}^{16} p(i) \frac{\log(p(i))}{\log(\frac{1}{16})} \dots\dots\dots(4)$$

The autocorrelation function is also used to characterize correlation between among the current and past samples of RR intervals. Practically this is estimated as provided in Equation (5).

$$\hat{\phi}_{xx}(\tau) = \frac{1}{R-\tau} \int_0^R x(t)x(t-\tau)dt \dots\dots\dots(5)$$

Thus, $\varphi_{xx}(\tau)$ is a measure of how correlated $x(t)$ is with its past value τ seconds earlier. Obviously, for noisy or broadband data, the autocorrelation at all delays other than 0 will be close to 0. This fact is utilized for the detection of AF from its RR interval series by taking the difference between the autocorrelation at delay 0 and at delay 1 and comparing
5 with some threshold. In addition, the autocorrelation at delay 0 is always normalized to 1 so as to enable comparison with a fixed and easy-to-compute threshold. A threshold of 0.02 was used for ACORR, that is any value that is greater than 0.02 is considered as AF.

In the present invention, a filtering of ectopic beats is preferably also performed. Ectopic beats occurring during regular sinus rhythm are a potential cause of erroneous
10 detection of AF since they confound all three components of the algorithm. Typically, a premature beat is characterized by the combination of a short coupling interval to the preceding normal RR interval, followed by a compensatory pause which is longer than both the ectopic coupling interval and the subsequent normal RR interval.

Thus, if the i -th RR interval is premature and the i -th+1 RR the compensatory
15 pause, then $RR[i-1] > RR[i] < RR[i+1]$ and $RR[i] < RR[i+1] > RR[i+2]$, yielding at least two additional turning points and three if $RR[i+1] > RR[i+2] < RR[i+3]$. In order to recognize the characteristic short-long RR interval sequence of ectopic beats a ratio $RR[i]/RR[i-1]$ is computed for each RR interval in the time series. For a regular sinus rhythm, this ratio is close to unity and fluctuations around it represent physiologic
20 variability. In the case of ectopy, the sequence of ratios is $RR[i]/RR[i-1] \leq 0.8$, $RR[i+1]/RR[i] \geq 1.3$, and $RR[i+2]/RR[i+1] \leq 0.9$. Preferably, rather than relying on an arbitrary fixed ratio, diverse ectopic beats with varying coupling intervals are captured by searching for RR sequences which satisfy the conditions $RR[i]/RR[i-1] < Perc1$ and $RR[i+1]/RR[i] > Perc99$ and $RR[i+1]/RR[i+2] > Perc25$ (where $Perc1$, $Perc99$, and
25 $Perc25$ are the first, 99th, and 25th percentile of RR ratios, respectively). When an ectopic beat is encountered, it is excluded from further analysis along with its compensatory pause.

The present invention utilizes the following threshold definitions. Optimal cut-
points for the algorithm of the present invention are identified by plotting the ROC for
30 RMSSD, selecting a threshold that optimizes sensitivity so that a maximum number of

possible AF beats can pass through to the next step. Such threshold definition minimizes the likelihood that true AF beats are filtered out in the first step of the analysis cascade.

In a preferred embodiment, a threshold of 9.8% of the mean RR interval of the 128-beat segment was used, based on inspection of the ROC, to yield a sensitivity and specificity of 99.1% and 79.33% for AF beats, respectively.

Next, keeping the RMSSD threshold fixed, a Turning Points analysis was added and a second ROC was constructed by varying only the confidence interval of the expected turning points ratio. As discussed above, the expected TPR of a random series is $0.666 \pm$ confidence interval. The ROC is obtained by varying the confidence interval of the TPR and plotting the corresponding sensitivity against the specificity. Again, the TPR threshold is selected so as to maximize the sensitivity without compromising on the specificity (e.g. this resulted in the sensitivity and specificity of 97.06% and 86.47% for AF beats, respectively).

Based on this analysis, sensitivity and specificity for AF detection are optimal for a confidence interval of the TPR between 0.527 and 0.8. Using the same approach for SE reveals the optimal cut point to be 0.8. For the AFIB database (N = 23 subjects), a threshold of 0.8 for the SE gave a sensitivity of 95.06% and specificity of 96.68% of all AF beats. Using the same criteria on the 200 series of the MIT BIH Arrhythmia database (N = 25 subjects) gave a sensitivity of 88.13% and a specificity of 82.01% for AF beats. For the 100 series in the same database (N = 23 subjects), the specificity was 98.38% for AF beats. Since there are no true AF beats in this series, the sensitivity cannot be quantified.

Testing was performed utilizing a 200 series of a MIT BIH Arrhythmia database (N = 25 subjects), which is the most challenging database because it contains many artifacts, including Atrial Premature Beats (APB), Ventricular Premature Beats (VPB). Removal of VPB prior to data analysis was found to increase sensitivity and specificity on the 200 series of the MIT BIH Arrhythmia database to 88.24% and 88.01% for AF beats, respectively.

For clinical applications, a most relevant objective is detection of AF in a given recording, not necessarily every single AF beat. Using this criterion, a sensitivity of

100% was achieved for both the AF and arrhythmia databases. The results of use of the present invention are summarized in Table 1, which provides AF detection accuracy.

Table 1

Database	AF beats (Sensitivity%/Specificity%)	AF episodes (Sensitivity%/Specificity%)
MIT-BIH AFIB (N=23)	93.51/97.03	100/99.11
MIT-BIH Arrhythmia 100 series (N=23)	NA/98.38 (note : no AF in this database)	NA
MIT-BIH Arrhythmia 200 series (N=25)	88.24/88.01	100/100
ScottCare Holter (N=23)	Not available	100/96

5 Furthermore, automatic real time detection of AF in a clinical setting appears feasible with the combined use of TPR, RMSSD and SE, as the algorithm takes only 2.5 seconds to compute 24-hour Holter data which contains approximately 100,000 beats. The only requirement of our algorithm is that at least 1.5-2 minutes of RR interval data are needed since the SE test requires 128 beats. The computation time of a 128-beat data
10 segment is on the order of 1-2 milliseconds.

Fig. 1 provides an example calculation of these statistics, along with the final detection using the corresponding thresholds for a sample recording from the MIT BIH Atrial Fibrillation database. Fig. 1(a) shows an episode of AF embedded in Sinus Rhythm from the MIT-BIH Atrial Fibrillation database is shown, Fig. 1(b) shows an
15 RMSSD, Fig. 1(c) shows a TPR, Fig. 1(d) shows SE, and Fig. 1(e) shows ACORR. Dotted lines in (b-e) represent threshold values as determined by the ROC. A final detection result as to whether an AF is detected is displayed in (f).

A recent analysis of 23 Holter recordings as provided by ScottCare Corporation, correct identification was made the presence of AF episodes in all subjects (sensitivity of
20 100% and specificity of 96%).

In another preferred embodiment of the present invention, a piezoelectric sensor is utilized to obtain RR intervals. This will facilitate a shift from current clinical practice of centralized AF detection (i.e. making the diagnosis at a doctor's office, clinic or hospital) to a distributed model relying on the patients themselves to obtain the data. The present
25 invention "piggy-backs" on daily blood pressure checks made at home, in a pharmacy, or even in select stores. In the preferred embodiment, a signal is acquired through a blood

pressure cuff adapted with an embedded piezoelectric sensor, to obviate the need for an electrocardiogram.

Fig. 4 shows a piezoelectric sensor incorporated into a blood pressure cuff for placement on a finger or on the brachial artery, and Fig. 5 provides a comparison of RR
5 intervals obtained from a commercial ECG device and PPV obtained via a piezoelectric sensor.

A preferred embodiment of the present invention embeds a piezoelectric crystal in a blood pressure cuff, as shown in Fig. 4. A signal from the piezoelectric crystal is utilized to obtain statistical criteria to diagnosis/exclude AF. In the preferred
10 embodiment, a peak systolic blood pressure is derived from successive heart beats. The preferred embodiment allows for remote patient monitoring in an essentially burden-free manner. The preferred embodiment allows diagnosis to be made of asymptomatic patients that is not addressed in conventional systems.

As shown in Fig. 5, a close correlation exists between ECG and piezoelectric
15 sensor derived signals. The device of the present invention does not impose an additional burden on the patient, other than an additional 3-5 minute data collection period. Moreover, since recording of an electrocardiogram with its attendant cost is avoided, since the piezoelectric sensor is reusable and does not require separate energy source, the incremental cost is minuscule compared to the potential public health benefit.

Fig. 6(a) shows a prototype of a wireless two-channel ECG circuit and Fig. 6(b)
20 shows wireless data collection of ECG developed in accordance with the present invention. Fig. 7 provides a flowchart summarizing data acquisition and the analysis algorithm.

While the invention has been shown and described with reference to certain
25 exemplary embodiments of the present invention thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the present invention as defined by the appended claims and equivalents thereof.

WHAT IS CLAIMED IS:

1. An Atrial Fibrillation (AF) analysis method comprising:
 - obtaining, in a real-time manner, an output that includes a patient heartbeat;
 - analyzing select consecutive obtained heartbeats;
 - 5 for each analyzed heartbeat, selecting a beat segment of RR intervals centered on that beat;
 - eliminating ectopic beats and compensatory pause associated with each ectopic beat;
 - calculating a root mean square of successive RR differences (RMSSD) of the beat
 - 10 segment;
 - performing a first identification that the beat segment is an AF candidate by determining whether the RMSSD is greater than a RMSSD threshold; and
 - if identified as an AF candidate, performing a second identification that the beat segment is an AF candidate by calculating a TPR of the segment and determining
 - 15 whether the TPR satisfies randomness criteria.
2. The method of claim 1, wherein the RMSSD threshold is a percentage of a mean RR interval of a 128 beat segment.
- 20 3. The method of claim 1, wherein the RMSSD threshold accounts for inherent data non-stationarity.
4. The method of claim 1, wherein the RMSSD threshold is not a constant and varies with each segment.
- 25 5. The method of claim 1, wherein the step of selecting a beat segment of RR intervals is selected from a 128 beat segment of RR intervals.
6. The method of claim 1, wherein the RMSSD is calculated by:

$$30 \quad \text{RMSSD} = \sqrt{\frac{1}{128} \sum_j^{j+l=1} (a(j+1) - a(j))^2} .$$

7. An Atrial Fibrillation (AF) analysis method comprising:

obtaining, in a real-time manner, an output that includes a patient heartbeat;

analyzing select consecutive obtained heartbeats;

5 for each analyzed heartbeat, selecting a beat segment of RR intervals centered on that beat;

eliminating ectopic beats and compensatory pause associated with each ectopic beat;

10 calculating a root mean square of successive RR differences (RMSSD) of the beat segment;

performing a first identification that the beat segment is an AF candidate by determining whether the RMSSD is greater than a RMSSD threshold;

if identified as an AF candidate, performing a second identification that the beat segment is an AF candidate by calculating a TPR of the segment and determining

15 whether the TPR satisfies randomness criteria; and

if again identified as an AF candidate, performing a third identification that the beat segment is an AF candidate by calculating a Shannon Entropy (SE) of the segment and determining whether the SE is greater than an SE threshold.

20 8. The method of claim 7, wherein the SE is calculated by:

$$SE = - \sum_{i=1}^{16} p(i) \frac{\log(p(i))}{\log\left(\frac{1}{16}\right)} .$$

9. An apparatus for detection of Atrial Fibrillation (AF), the apparatus comprising:

25 a blood pressure cuff; and

a piezoelectric sensor imbedded in the blood pressure cuff;

wherein, real-time output is provided that includes a patient heartbeat,

consecutive heartbeats are analyzed and a beat segment is selected of RR intervals centered on each beat,

ectopic beats and compensatory pause associated with each ectopic beat are eliminated by calculating a root mean square of successive RR differences (RMSSD) of the beat segment, and identifying whether the beat segment is an AF candidate by determining whether the RMSSD is greater than a RMSSD threshold.

5

10. The apparatus for AF detection of claim 9, wherein if an AF candidate identification is made, a second identification is performed by calculating a TPR of the segment and determining whether the TPR satisfies randomness criteria

10

11. The apparatus for AF detection of claim 9, wherein if an AF candidate identification is again made, a third identification is performed by calculating a Shannon Entropy (SE) of the segment and determining whether the SE is greater than an SE threshold.

15

12. The apparatus of claim 9, wherein the RMSSD threshold is a percentage of a mean RR interval of a 128 beat segment.

20

1/7

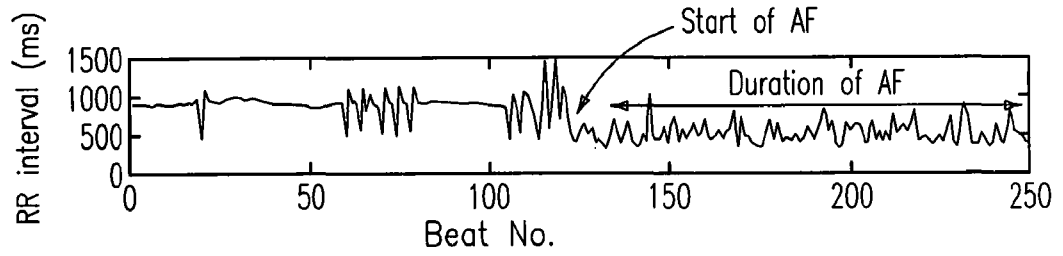


FIG. 1(a)

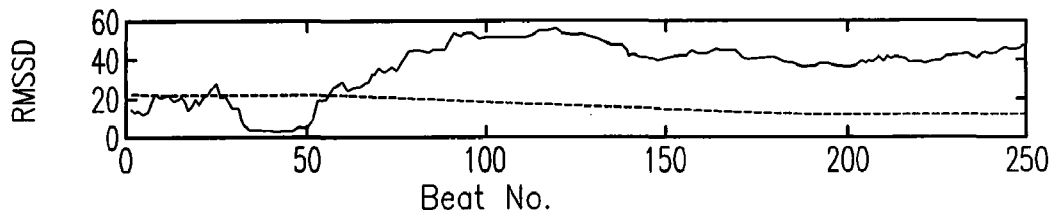


FIG. 1(b)

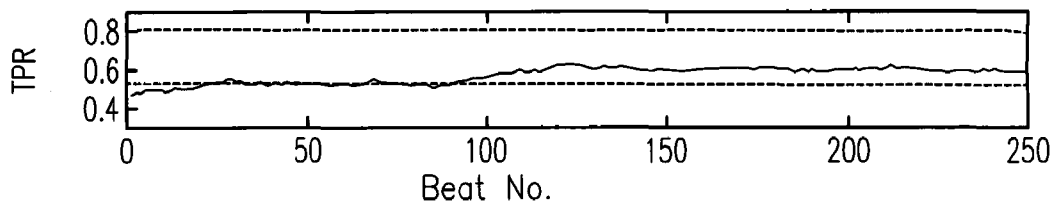


FIG. 1(c)

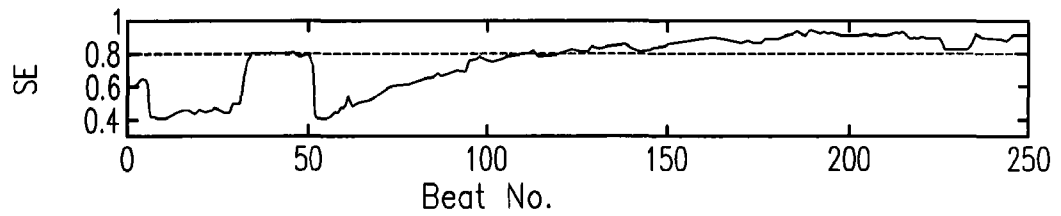


FIG. 1(d)

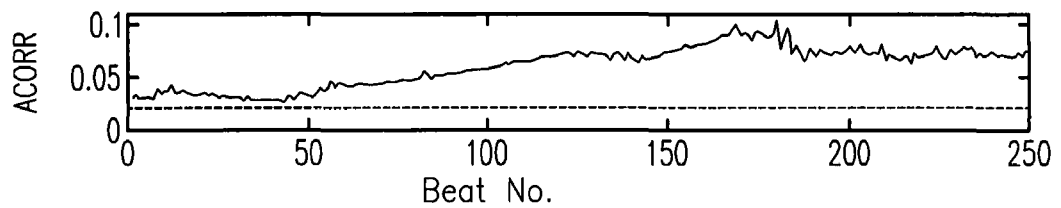


FIG. 1(e)

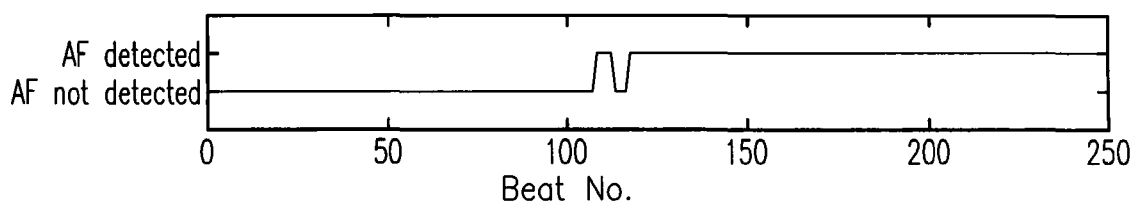
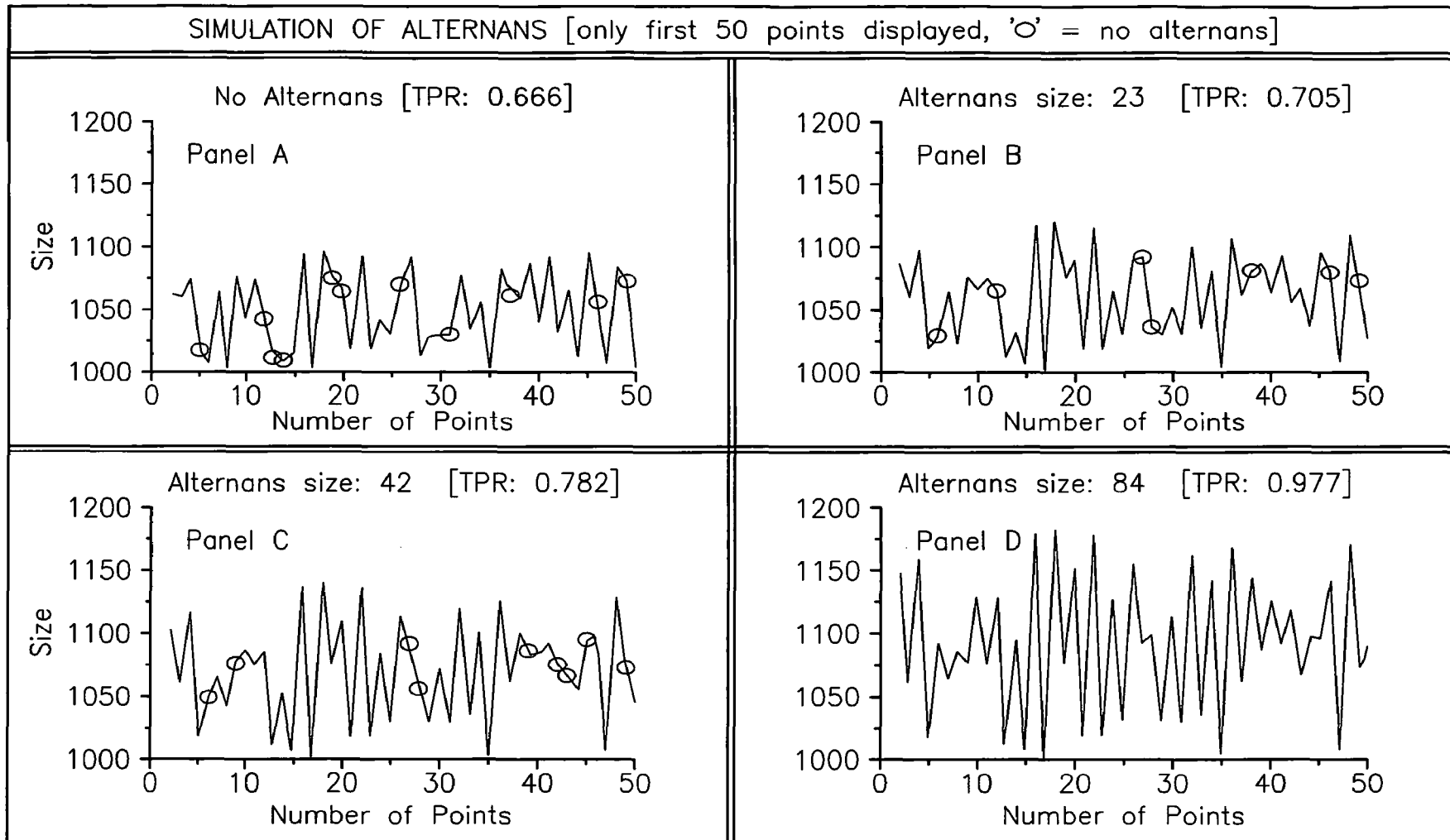


FIG. 1(f)



2/7

FIG. 2

3/7

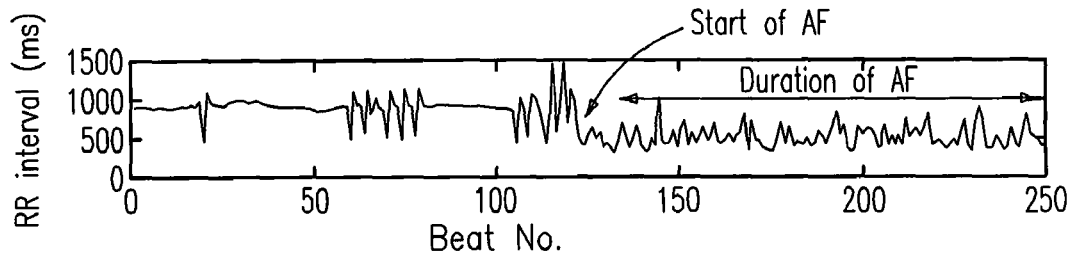


FIG. 3(a)

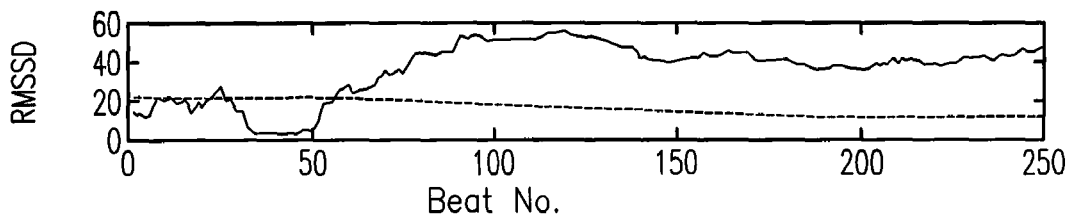


FIG. 3(b)

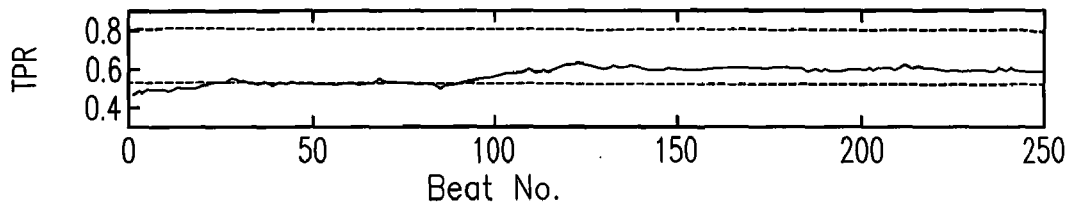


FIG. 3(c)

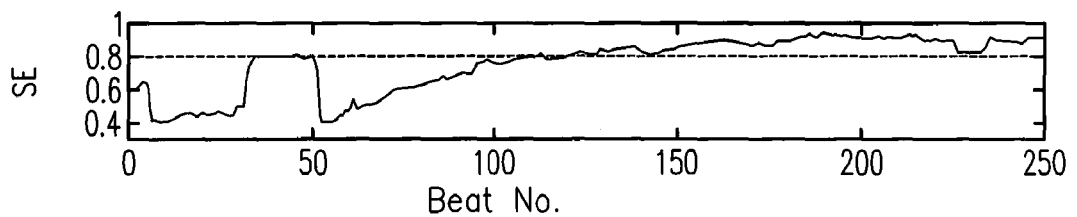


FIG. 3(d)

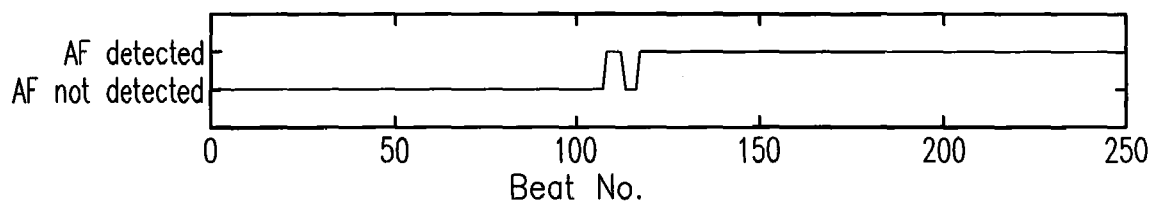


FIG. 3(e)

4/7

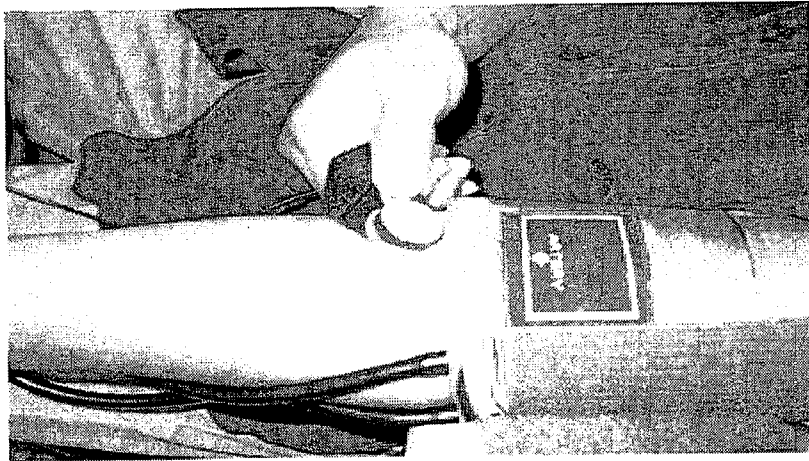


FIG. 4

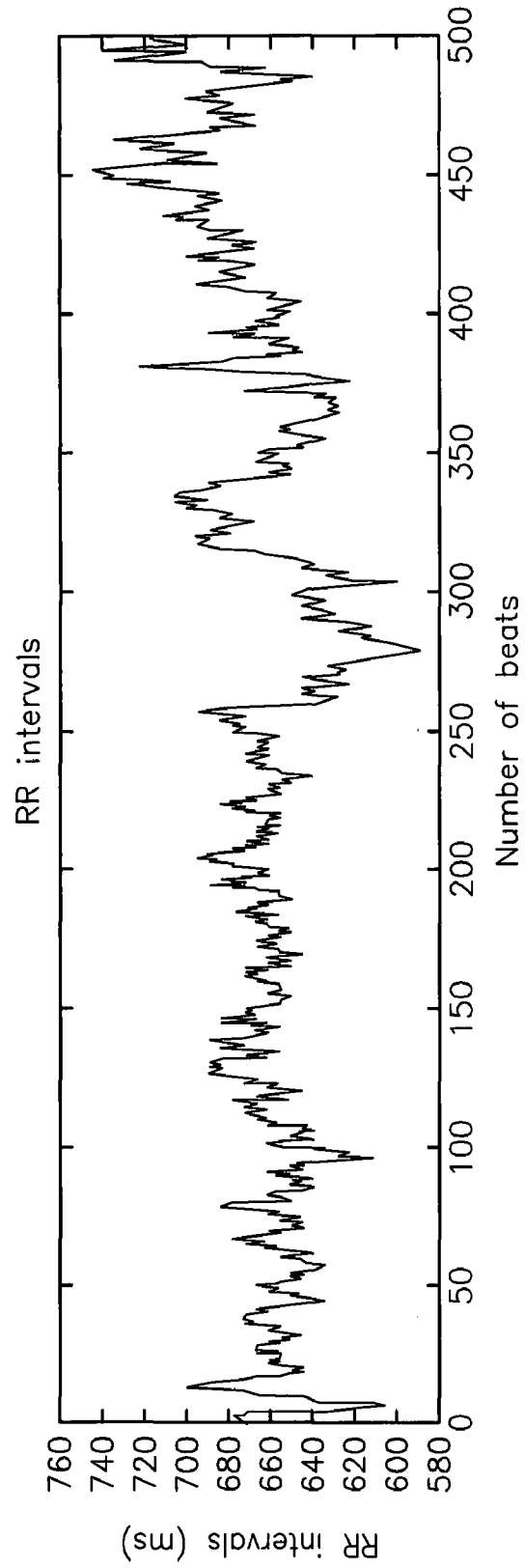


FIG. 5

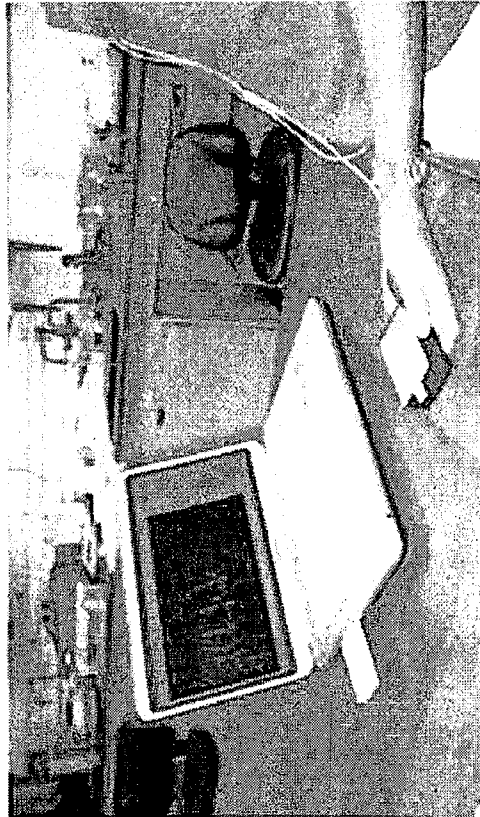


FIG. 6b

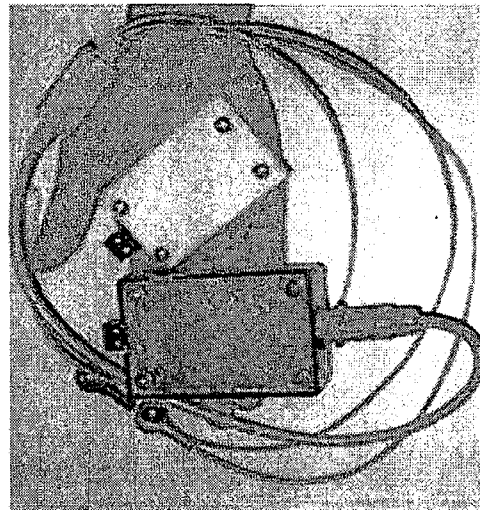


FIG. 6a

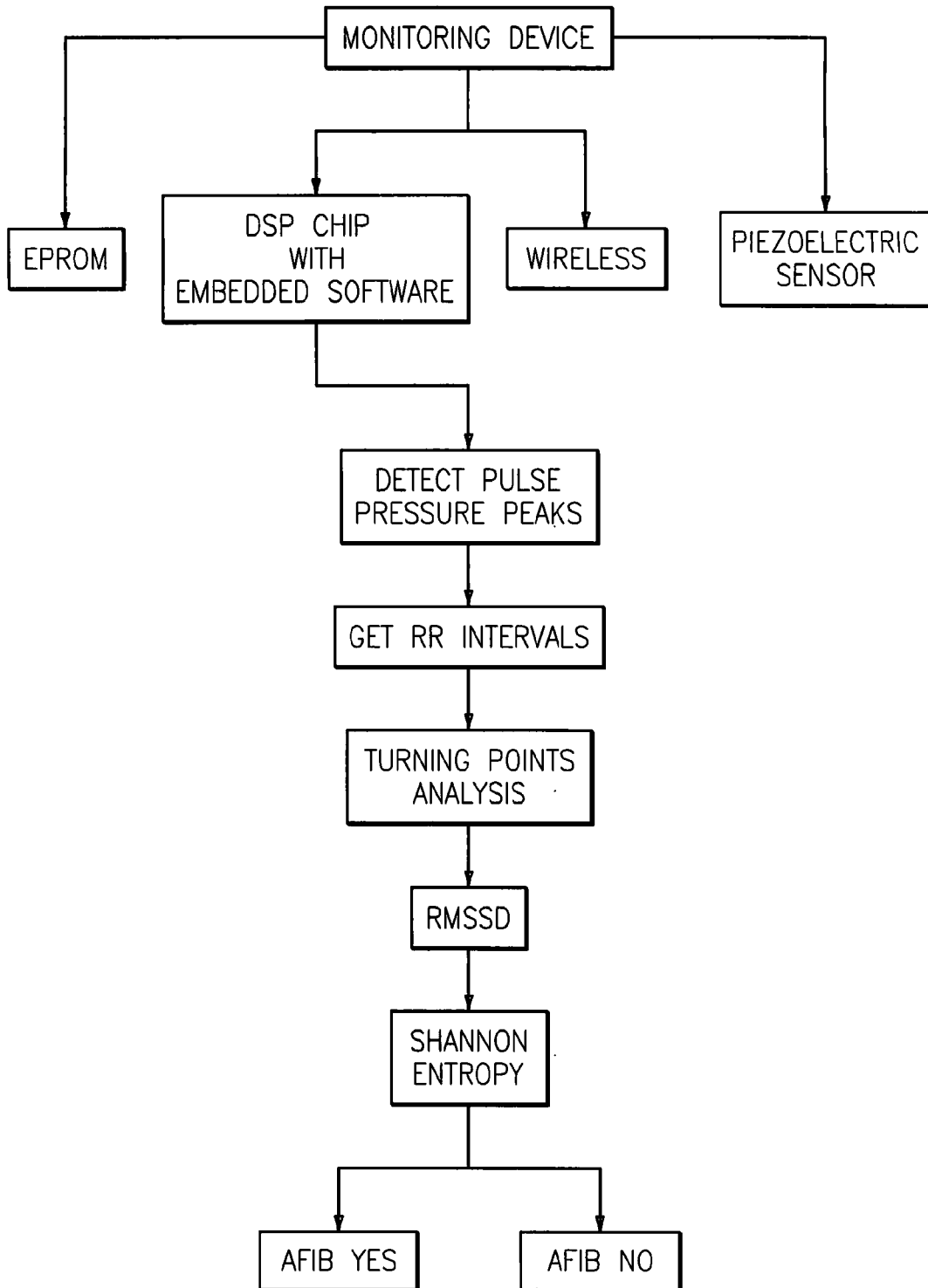


FIG. 7