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Long QT Syndrome Diagnosis and Classification

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Field

This invention relates to methods for detecting and diagnosing cardiac disease in a subject.

More specifically, the invention relates to diagnosing and classifying long QT syndrome in

1

In clinical practice, QT interval is the only standard and universally accepted quantitative measure used for non-invasive diagnosis of LQTS. It is usually measured by an ECG specialist manually, using one of the well-known formulas such as Bazett's formula [3]:

$$QTc = \frac{QT}{\sqrt{RR}}$$

where QT and RR represent the QT and RR intervals in seconds, and QTc represents the heart-rate-

corrected QT interval. If the maximum QTc measured in an ECG is greater than a threshold (450 ms in males and 470 ms in females), it is typically considered as LQTS [4].

10 However, measuring the QT interval this way is a time-consuming process which is subject to human error. In fact, statistical analysis reveals that only 50% of cardiologists know how to measure it appropriately [5]. This is because a universally accepted mathematical definition of the onset and/or end point of the T wave does not exist, resulting in a high inter- and intra-analyst variability due to subjective nature of the measurements. Moreover, due to the low signal to noise ratio and low amplitude of the T

Summary

One aspect of the invention relates to a method for detecting long QT syndrome in a subject

The method may comprise further classifying a LOT syndrome ECG signal as a LQTS1 ECG signal

or a LQTS2 ECG signal.

The method may comprise subjecting the LOT syndrome ECG signal to logistic regression based

on a set of features related to T wave morphology.

5 In one embodiment, the set of features related to T wave morphology comprise number of local

peaks, base of the T wave, and difference between the slopes at their boundaries

FIG. 3A 3D surface diagram showing different CT interval measurement methods.

threshold (TH), differential threshold (DTH), slope intercept (SI), and peak slope intercept (PSI), respectively.

FIG. 4 is a plot showing an ECG signal with baseline wandering, wherein dots represent inflection points extracted using equation (3) presented herein, and shaded areas show the truncated energy

FIGs. 3A-3D show various clinical approaches practiced by cardiologists for finding the onset/offset of the QRS complex and the T-wave, including amplitude threshold (TH; FIG. 3A)

differential threshold (DTH; FIG. 3B), slope intercept (SI; FIG. 3C), and peak slope intercept (PSI; FIG. 3D)

FIG. 3E is a comparison of these methods; the SI method is the most reliable in clinical

$$y_n = \text{LoG}_n^{(\sigma)} * x_n \quad (2)$$

in which $*$ represents the convolution. The IPs are then identified by locating the zero-crossings of y_n :

$$z_m = \{1 \leq n \leq N \mid y_n = 0, y_{n-1} < 0\} \quad m = 1 \dots M \quad (3)$$

In the embodiment described below, four features were selected for the multi-dimensional

space: duration M , energy E , distance D , and standard deviation S . These are described in detail

their truncated energy is almost equal ($E_i \approx E_j$). Moreover, the isoelectric segments represent a very low truncated energy while their energy may be high due to baseline variations. This guarantees that ECG waves would fall under the same categories in terms of E_m , regardless of baseline wandering.

5 boundaries was used as another feature in the analysis:

features is explored. This is because the natural logarithm corresponds for clustering of the features

technique, a new set of features based on the IPs is set forth herein:

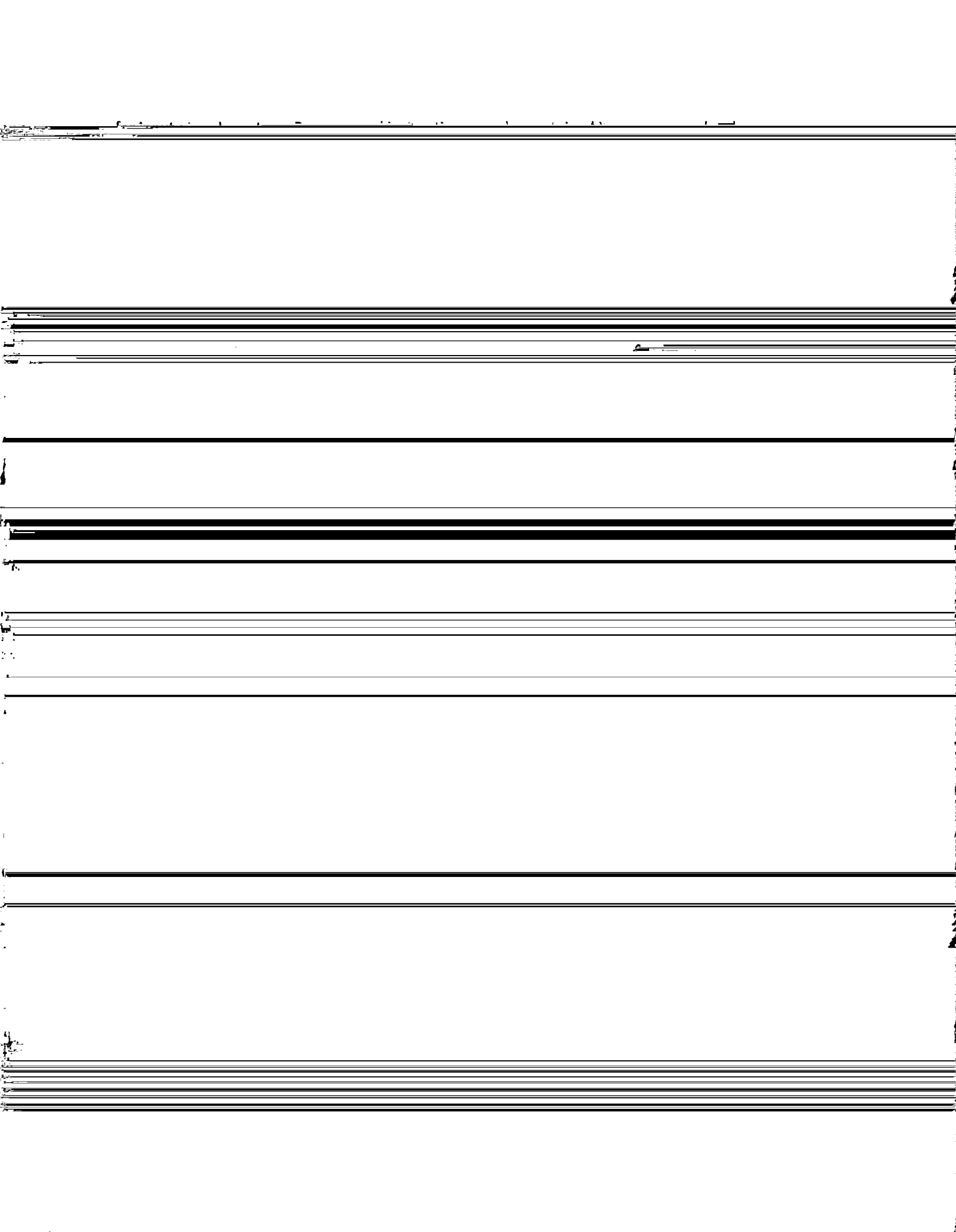
- 1) *QT Interval*: The first feature that needs to be measured is the QT interval. As mentioned above, there are multiple clinical approaches for finding the onset/offset of QRS complex

4) *Slopes at IPs:* The slopes of the T wave at its IPs are used as two new features. These

features are represented by the slopes of lines l_1 and l_2 in FIG. 7. The ratio of the difference between

The slope of these two lines is another morphological feature that represents the symmetry between

standard deviation of the features is used in the calculations. Hence, for every feature introduced in the method there are two values: mean and standard deviation, making the feature space twice as large



REFERENCES

[1] J. P. Hampton, *The ECG Made Easy*, Elsevier Health Sciences, 2012.

Claims

1. A method for detecting long QT syndrome (LQTS) in a subject, comprising:

obtaining data corresponding to an electrocardiogram (ECG) signal of the subject;

identifying a set of features in the data based on selecting inflection points of the ECG signal by

8. The method of claim 7, wherein the four dimensional feature space for an ECG segment

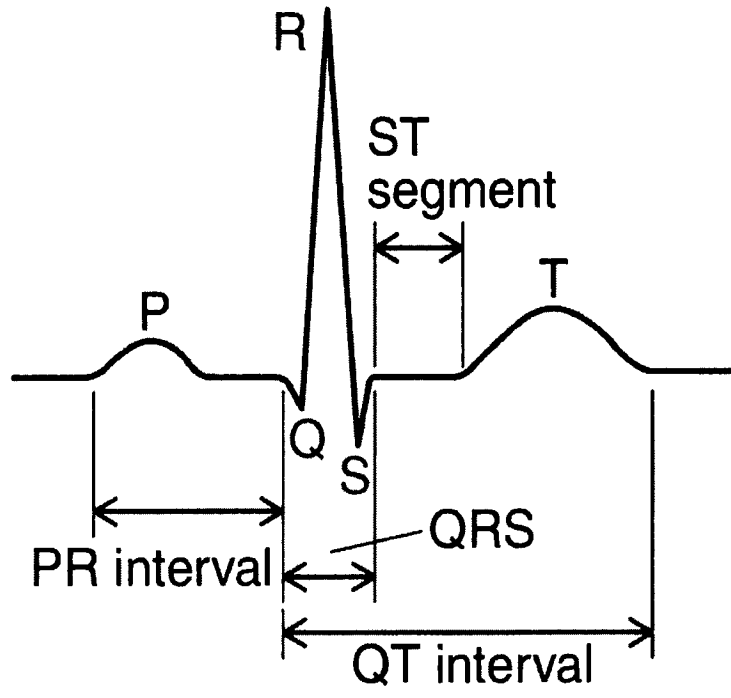


FIG. 1 (PRIOR ART)

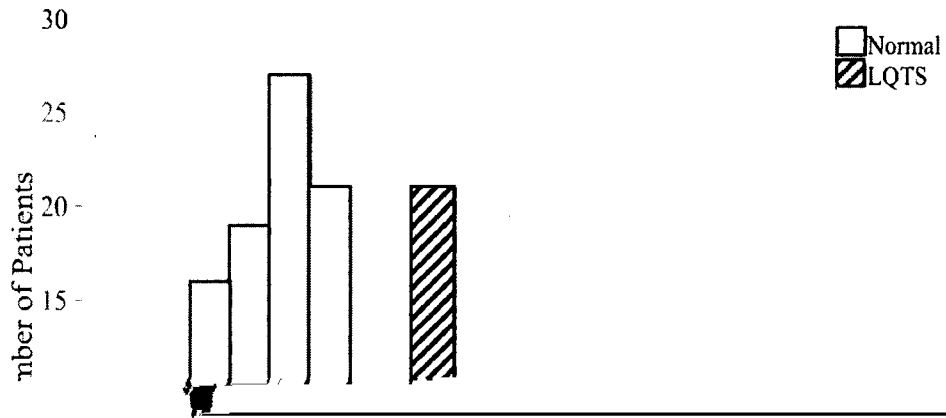
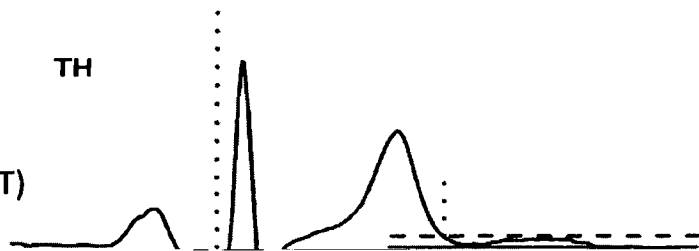


FIG. 3A
(PRIOR ART)



250

200

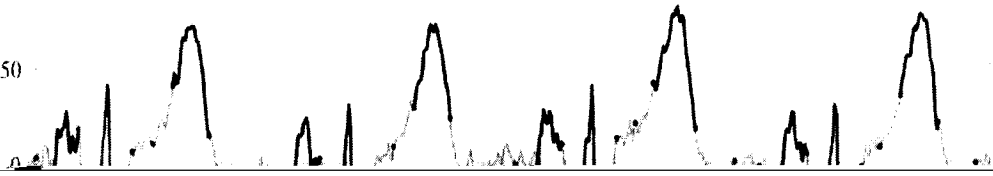


Distance (Vertical)

1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1

EM

50



R



$L_{z_{k+1}}$



[Redacted]

NORMAL

[Redacted]

[Redacted]

[Redacted]

[Redacted]

True Classes	Normal	30	
	LQTS		20

Predicted Classes

FIG. 10A

Classes	Type 1	10	
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Abstract

A method for detecting long QT syndrome in a subject comprises obtaining data corresponding to an electrocardiogram (ECG) signal of the subject, identifying a set of features corresponding to

selected inflection points of the ECG signal, using the set of features to categorize segments of the ECG signal, and using the categorized segments of the ECG signal and the inflection points to classify the ECG

