

EFFECT OF EXERCISE ON QT DISPERSION

A THESIS

SUBMITTED TO THE DEPARTMENT OF ELECTRICAL AND
ELECTRONICS ENGINEERING
AND THE INSTITUTE OF ENGINEERING AND SCIENCE
OF BILKENT UNIVERSITY
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER OF SCIENCE

By

LOTTU ÜZGÖR
December 1998

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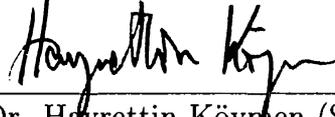
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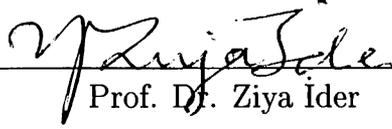
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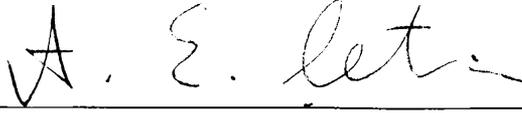
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ABSTRACT

EFFECT OF EXERCISE ON QT DISPERSION

Lütfü Özçakır

M.S. in Electrical and Electronics Engineering

Supervisor: Prof. Dr. Hayrettin Köymen

December 1998

Electrocardiogram (ECG) is the measurement of potential differences occurring on the body due to the currents that flow on the heart during diastole and systole. Cardiac abnormalities cause uncommon current flows, leading to strange waveform morphologies in the recorded ECG. Since some abnormalities become visible in ECG only during activity, exercise ECG tests are conducted.

Among all abnormalities, exercise induced ischemia is considered in this study. The previous studies have shown that exercise induced ischemia increases the QT dispersion (QTD).

The patients in this study have been validated by cardiologists using ST segment analysis. However, the sensitivity and specificity of ST segment analysis is low. Some of the patients have been validated as ischemic using the coronary angiography results.

A different method to measure the QT interval through out the exercise ECG test has been developed . The algorithm is designed to cope with the artifacts of exercise ECG. Such as high noise level and PT fusion. A different approach to obtain the QTD has been developed. We have shown that, QTD increases significantly in patients who have ischemia during exercise. The sensitivity and specificity of exercise ECG test can be increased if QTD analysis is used as an additional tool to ST analysis.

Keywords : Exercise ECG, QT interval, QT Dispersion

ÖZET

EFORUN QT BOZULUMU ÜZERİNE ETKİSİ

Lütfü Özçakır

Elektrik ve Elektronik Mühendisliği Bölümü Yüksek Lisans

Tez Yöneticisi: Prof. Dr. Hayrettin Köymen

Aralık 1998

Elektrokardiyogram (EKG), kalpten sistol ve diyastol sırasında yayılan elektrik akımlarının vücudun yüzeyinde oluşturduğu potansiyel farkların ölçümüdür. Kardiyolojik bozukluklar EKG'de normal olmayan morfolojilere neden olurlar. Bu anormalilerden bazıları sadece aktivite sırasında gözlenebildiği için Eforlu EKG Testi uygulanmaktadır.

Bu çalışmada, bütün bu kardiyolojik bozuklukların arasından efor ile oluşan iskemi göz önüne alınacaktır. Daha önceki çalışmalar, efor ile oluşan iskeminin QT bozulumunu (QTB) arttırdığını göstermişlerdir.

Bu çalışmadaki hastalar, ST aralığı analizi kullanılarak, kardiyologlar tarafından onaylanmışlardır. Ancak ST aralığı analizinin hassasiyeti ve ayırcılığı düşüktür. Buna ilaveten, bazı hastalar koroner anjiyografi sonuçları kullanılarak iskemik olarak onaylanmışlardır.

Bütün eforlu EKG testi sırasında QT aralığını ölçmek için, farklı ve yeni bir metod geliştirilmiştir. Algoritma eforlu EKG bozuklukları ile başa çıkabilecek şekilde tasarlanmıştır. Yüksek gürültü seviyesi ve PT birleşimi bu bozukluklara örnektir. Ayrıca QTB'yi elde etmek için farklı bir yaklaşım sunulmuştur. QTB'nin aktivite sırasında iskemisi olan hastalarda dikkate değer bir şekilde arttığını gösterdik. Eğer, QTB analizi, ST aralığı analizine ek bir araç olarak kullanılırsa, eforlu EKG testinin hassasiyeti ve ayırcılığı arttırılabilir.

Anahtar Kelimeler : Eforlu EKG, QT aralığı, QT bozulumu,

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Chapter 1

Introduction

1.1 Objective of the study

The diagnosis of coronary artery disease (CAD) in subjects with chest pain is a difficult problem in clinical medicine. Exercise ECG testing has a limited value in the detection of CAD (especially in female population) due to excessive false positive results [2]. Depending on disease prognosis, the false positive rate changes from % 25 to % 50 in patients with typical chest pain [3].

The QT interval is the interval from the beginning of ventricular depolarization (Q point in the ECG) to the end of the ventricular repolarization (end of the T wave) and is sensitive to myocardial ischemia. The interlead variation in the 12-lead (or the measured leads) is called QT dispersion (QTD). QTD reflects the inhomogeneity in the duration of myocardial repolarization and is increased in patients who have ischemic heart disease and myocardial infarction.

Numerous investigations are being done for the identification of the patients at risk of sudden cardiac death. Most of the sudden deaths are due to ventricular tachycardia or ventricular fibrillation.

If a part of the heart can not get enough blood due to narrowed arteries; this part has been injured or dead. The heart is then called to *have ischemia*. These injured or dead parts can not give enough electrical response to hormones which stimulate the heart to beat faster during exercise as well as the healthy parts [4]. This phenomenon causes different timing of repolarization between healthy and injured parts. Different timing of repolarization between neighboring areas of the heart causes ventricular arrhythmia by allowing current eddies and reentrant tachycardia via microcircuits within the ventricle. Nonuniform myocardial repolarization time may result from inhomogeneity of action potential duration due to slow conduction or altered conduction pathways through the heart [5]. Assessment of this inhomogeneity should be done using the standard 12-lead ECG's fiducial points like Q,T.

The maximum QT interval should be measured from the beginning of the QRS complex to the end of the latest T wave among all leads of a simultaneous 12-lead ECG recording. This approximates the time from the earliest depolarization of ventricular myocardium to its latest repolarization. Beginning of the QRS complex is approximately the same for all leads thus measuring the T waves' end is important. The QT interval has long been known to vary significantly between the individual leads of the 12 lead ECG, [6] but in 1990 a potential application of this interlead difference was proposed by Day et al. [4]. These authors suggested that if individual leads reflect the regional activity, the interlead difference in QT interval may provide a measure of repolarization inhomogeneity. They called this interlead difference as *QT Dispersion*. Figure 1.1 shows this definition. The time interval between last 2 vertical lines shows QT Dispersion definition. The spikes show Q point, S point, J point, beginning of T wave, T peak and end of T wave respectively.

In most studies [7], QT dispersion has been defined as the difference between the maximum and minimum QT intervals measured from each of the 12 standard leads. However the standard deviation (SD) of QT intervals may provide a more reliable measure of dispersion since it does not depend on the number of leads measured. Hanakova [8] found that the SD of the QT interval is less effected by the number of the missing leads.

Since the QT interval shortens as the heart rate increases, numerous formulas have been derived in order to reduce the effect of heart rate increase

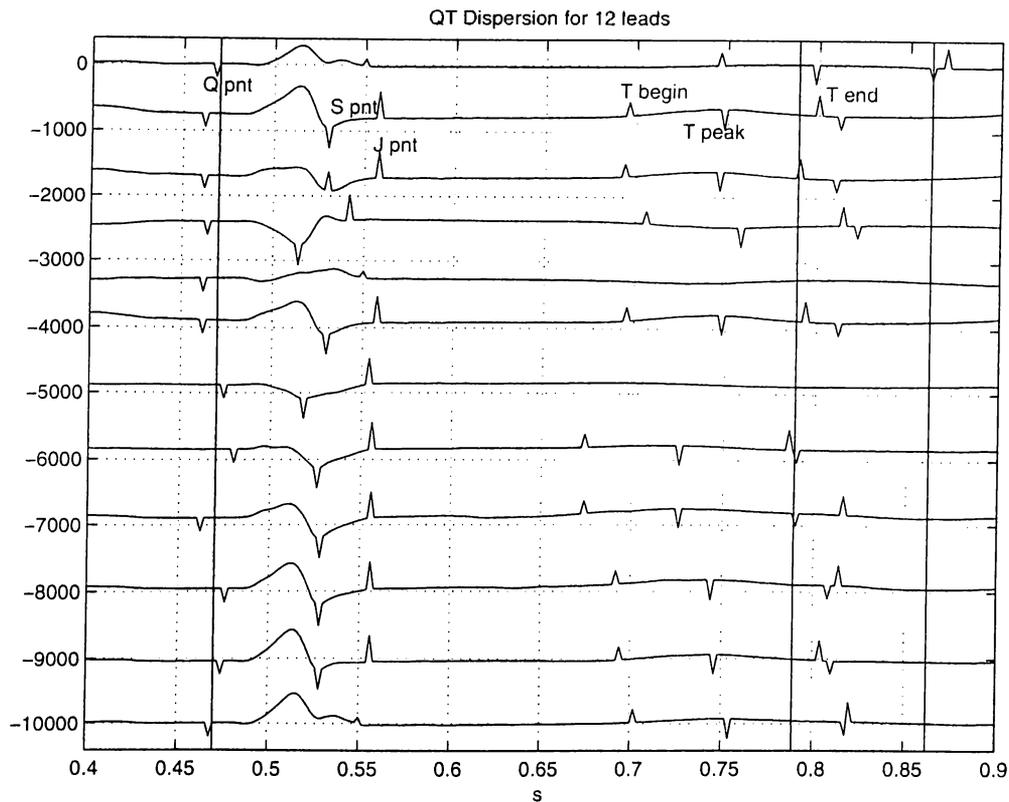


Figure 1.1: QT dispersion definition

and compare the measurements, which have been done at different heart rates. These formulas are assumed to correct the QT interval with respect to heart rate. The frequently used formulas are Bazett's formula [9] and Framingham Heart Study QT interval correcting formula [10]. The corrected measurements are shown as QT_c . Equations 1.1 and 1.2 shows Bazett's and Framingham correcting formulas respectively.

$$QT_c = QT + \frac{QT}{\sqrt{RR_{int}}} \quad (1.1)$$

$$QT_c = QT + 0.154(1 - RR) \quad (1.2)$$

These formulas are derived for heart rates less than 120 bpm, hence it is not appropriate to use them for exercise ECG. Thus in this study no comment has been done on corrected QT Dispersion [10]. These calculations may lead to

increased QT_c dispersion during higher heart rates and influence the diagnosis made for the patients who have a higher heart rate due to illness.

QT dispersion provides a measure of arrhythmia risk too [10]. Thus it can be used to detect the patients who will have arrhythmia during exercise.

The exercise ECG test records used in this study have been read by the cardiologists in the hospital. They have validated the records using ST segment analysis. In our research an exercise test is diagnosed as POSITIVE by the cardiologist if a ST segment depression $\geq 1mm$ occurs in 3 consecutive beats, in 2 leads at least. Also the other parameters such as age, sex and history are considered. The diagnosis of exercise tests is done by cardiologists in Ibni Sina Hospital, Cardiology Dept. Some of the patients who have a positive exercise ECG test had undergone coronary angiography to make the final diagnosis about the coronary arteries.

Cumming et. al [11] reported that ST segment changes in % 25 to % 66 of women confuses the interpretation of routine treadmill exercise test. The sensitivity and specificity of treadmill exercise test when diagnosing the ischemic heart disease is not high if we use only the ST segment changes.

Our hypothesis is that exercise-induced myocardial ischemia can increase QT interval in the regions of ischemia and give rise to an increase in QTD in the 12-lead ECG. The QTD analysis can improve the diagnostic accuracy of exercise ECG test when used with ST segment analysis. Since it is known that exercise induces ischemia in the heart, assessing the QT dispersion during exercise can give useful information for the diagnosis of ischemic heart disease.

A different approach and algorithm for the measurement of QT interval and formation of QT dispersion are proposed in order to reduce the effects of measurement errors in the analysis. The QT interval measurements have been done throughout the whole exercise test. The formation of the QTD is also different from previous approaches. The artefacts are exercise specific such as T-P wave fusion, muscle noise (EMG) and baseline wander (electrode movement). The algorithm was designed to cope with these artefacts. This algorithm is immune to noise and PT fusion. The proposed method is designed to run in real time and can be installed into a real-time ECG machine program

easily without effecting the operation of program.

The fiducial points found by the algorithm are visually verified. During verification, the computer program of Massachusetts Institute of Technology (MIT) and Beth Israel Hospital (BIH) has been used. All of the beats are viewed by this program. The algorithms are improved as a result of verification.

We have seen that QT dispersion increases significantly in patients with ischemic heart disease (approved by coronary angiography results for some patients) and decreases in patients who had drug or surgical therapy such as Percutaneous Transluminal Coronary Angioplasty (PTCA) and stent. These are two methods to reperfuse the veins and decreases the level of ischemia.

1.2 Outline

In this study the effect of exercise induced ischemia on QT dispersion is investigated during a standardized exercise ECG test.

Chapter 2 presents a review on exercise electrocardiography followed by the description of previous studies and clinical value of the QT dispersion.

In Chapter 3, the methods and materials used in this study are presented. First a section on data acquisition and QRS complex detection is presented. Next, composing average beats, filtering, finding the fiducial points is discussed. Measuring the QT interval and elimination of the measurements are also discussed in this chapter.

In Chapter 4 the statistical elimination and process of the measurements are discussed. The difference of the study from the previous studies has been shown here.

In Chapter 5 we present the results of the study. We describe the patient set and present the QT dispersion plots of these patients. Also conclusions have been made on these patients. As the last step a short section for the future study is presented.

A CDROM including all the related software and data has been prepared. The flowchart of the whole algorithm is presented in chapter 3. In Appendix A, the plots of QT dispersion plots for all patients have been given.

Chapter 2

A Review on Exercise ECG and QT Dispersion

2.1 Exercise Electrocardiography

ECG is the recorded electrical potential generated by the heart during a cardiac cycle. An electrical impulse passes through the tissues causing small amount of electrical currents spreading all the way to the surface of the body. These currents generate the electrical potentials recorded in ECG. Figure 2.1 shows the location of the ECG recording leads on the body.

The normal ECG is composed of a P wave, a QRS complex and a T wave. QRS complex is actually three separate waves, the Q, R and S waves. J point is end of the QRS complex. All of them are caused by the depolarization of the ventricles when the impulse is propagating. T wave is a result of repolarization of the ventricles. Before a new depolarization of ventricles start, repolarization must end. In other words the T wave peak is always before the Q point of new coming beat. This is a physical fact and will be used while defining T wave peak search window.

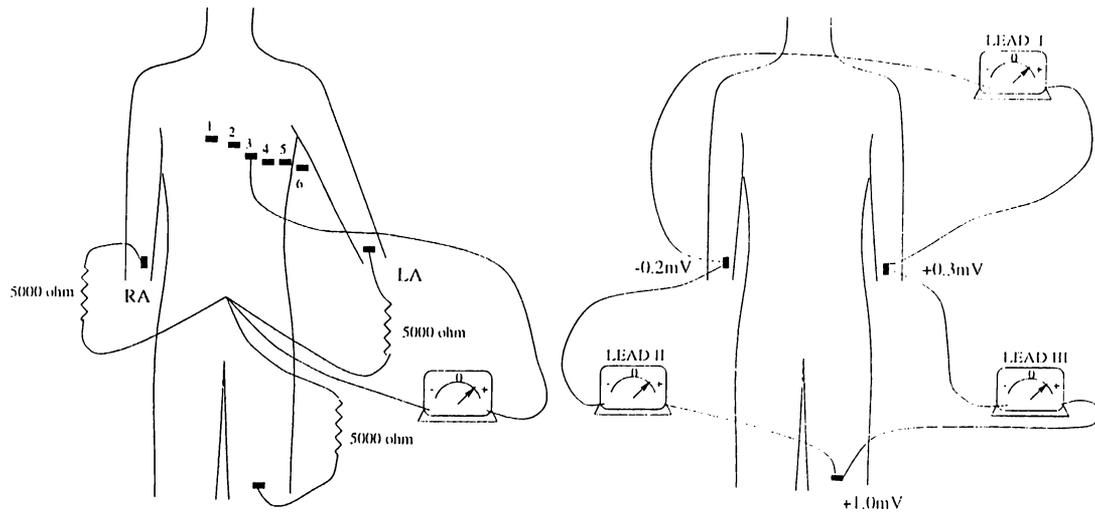


Figure 2.1: Standard leads used in ECG recording

Figures 2.2 and 2.3 show typical heart beats recorded from standard 12-lead channels.

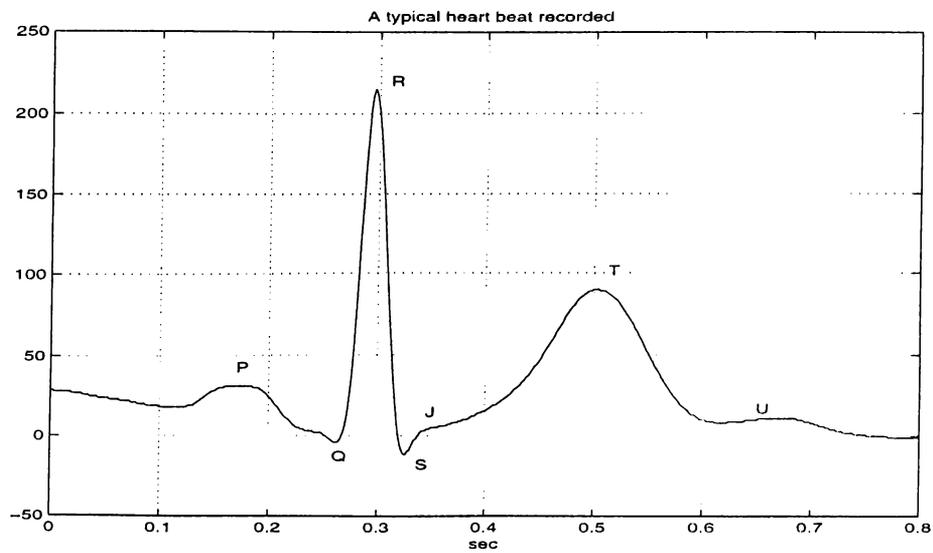


Figure 2.2: Typical heart beat

The exercise electrocardiography (stress ECG test or exercise ECG test) is one of the most important non-invasive diagnostic tests in the clinical evaluation and management of patients with cardiovascular disease, particularly coronary artery disease or ischemic heart disease. The exercise ECG test is primarily used for the assessment of the chest pain and for the early detection

of the coronary artery disease. Ischemia is caused due to decreased blood flow to myocardia from the heart arteries. Heart arteries are called "*Coronaries*"

In addition, the exercise ECG test can provide valuable information in evaluating the capacity of the patients with CAD, also in evaluating the efficiency of medical or surgical therapy [12].

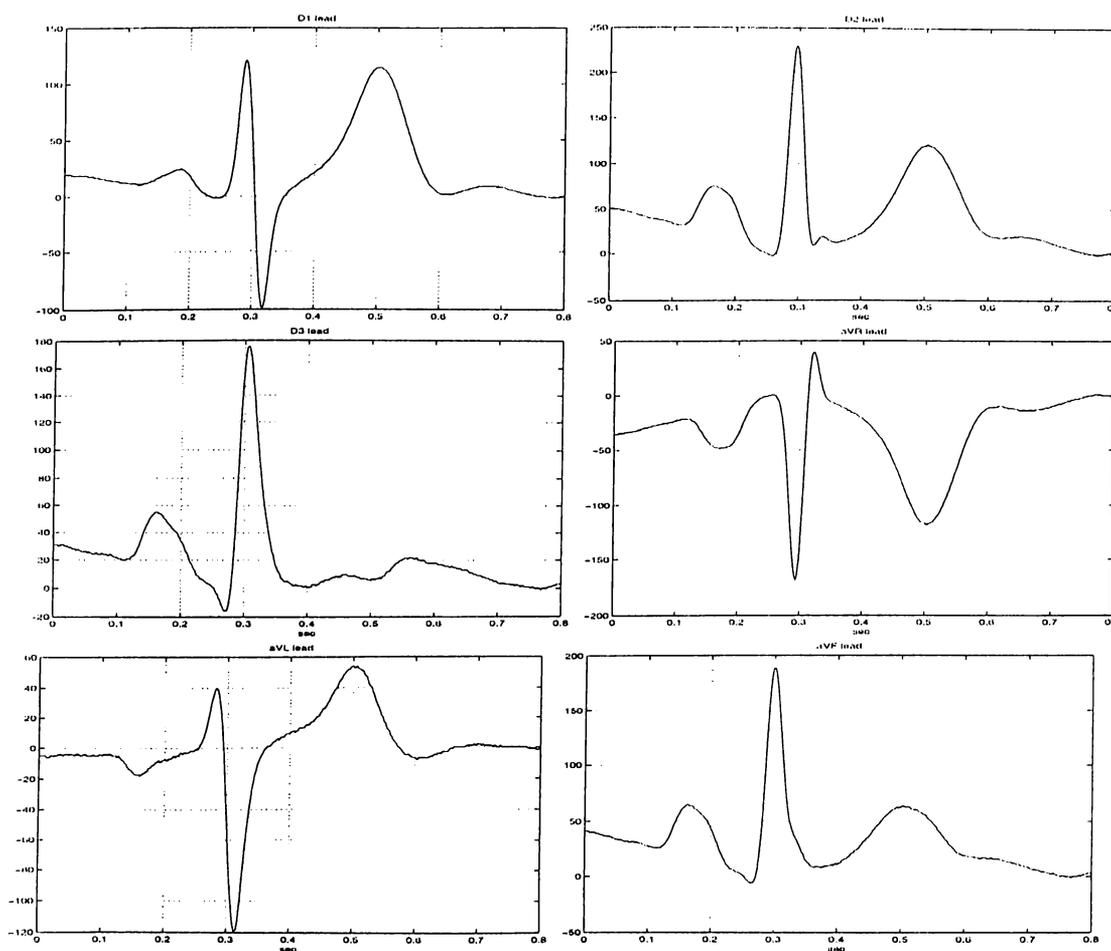


Figure 2.3: Typical beats recorded

Exercise protocols have been developed by different investigators for the exercise ECG test using either a treadmill or a bicycle ergometer. The following are valuable contributors of modern exercise ECG: Astrand, Balke, Blackburn, Bruce, Clausen, Ellestad, Epstein, Fox, Froelicher, Kattus, McHenry, Naughton, Sheffield and many others [12]. In 1956 modern exercise ECG tests

using motor driven treadmill began to receive wide acceptance for research purposes as well as clinical medicine. At present the treadmill is the most popular method of exercise testing.

Although various exercise protocols are designed by different investigators, none of these are ideal and can be modified for special purposes. In some protocols, the work load is increased by changing the speed at a fixed inclination (Astrand) where as in others the incline is increased while speed is fixed. The workloads should be increased gradually and maintained for a sufficient length of time to achieve a near physiological state.

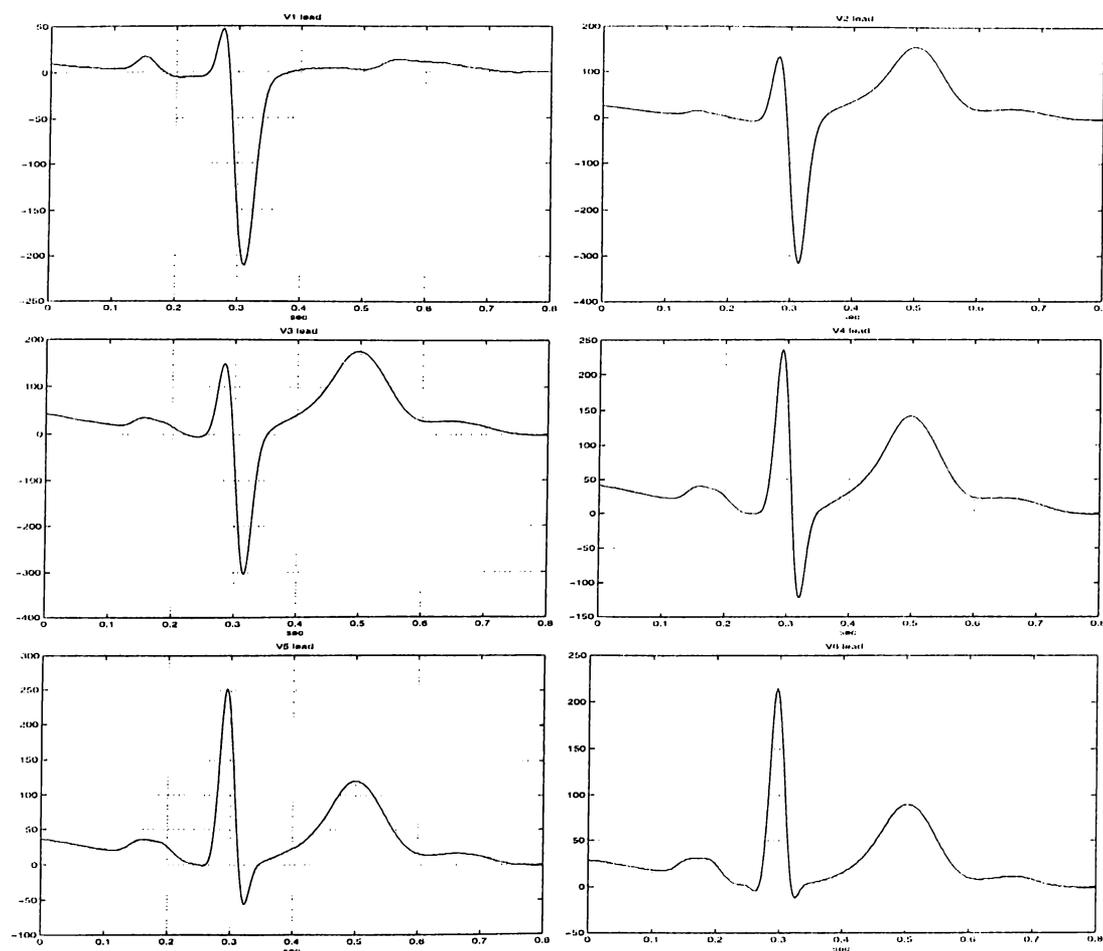


Figure 2.4: Typical beats recorded

In Bruce protocol both the speed and inclination is increased every three minutes in each of the seven stages. It is relatively short in duration but has the disadvantage of having very heavy exercise workloads for cardiac patients

or elderly individuals. Table 2.1 shows the steps of the Bruce protocol. In this study all patients had undergone a Bruce protocol exercise ECG test.

Stage	Grade	Speed (km/h)	Total Time
1	10	2.8	3
2	12	4.2	6
3	14	5.6	9
4	16	6.8	12
5	18	8.3	15
6	20	9.1	18
7	22	10	21

Table 2.1: Bruce Protocol Steps

2.2 Definition of the End of the QT Interval

Definitions of the end QT interval vary between studies [5]. Definitions are:

1. the return of T wave to isoelectric line,
2. the nadir between the T wave and the following U wave, and
3. the intersection of a tangent line to the downslope of the major repolarization wave (T wave) with the baseline.

Figure 2.5 shows different T wave end definitions and the process done by the cardiologists to detect the T wave end.

It is very difficult to see the U wave in exercise ECG because the signal to noise ratio (SNR) is low. The effect and the cause of the U waves are not very clear so the second definition is not used in this thesis. We eliminate the first definition because very high heart rates are considered in this study. T wave's return to baseline is not seen since a PT fusion occurs. We have used the third definition, which gave the best results since it uses Least Squares approximations while fitting the tangent line to the downsloping part of T wave.

The relationship between QT Dispersions measured using different definitions for the end of the QT interval is unclear. Kautzner et. al. [13] have shown

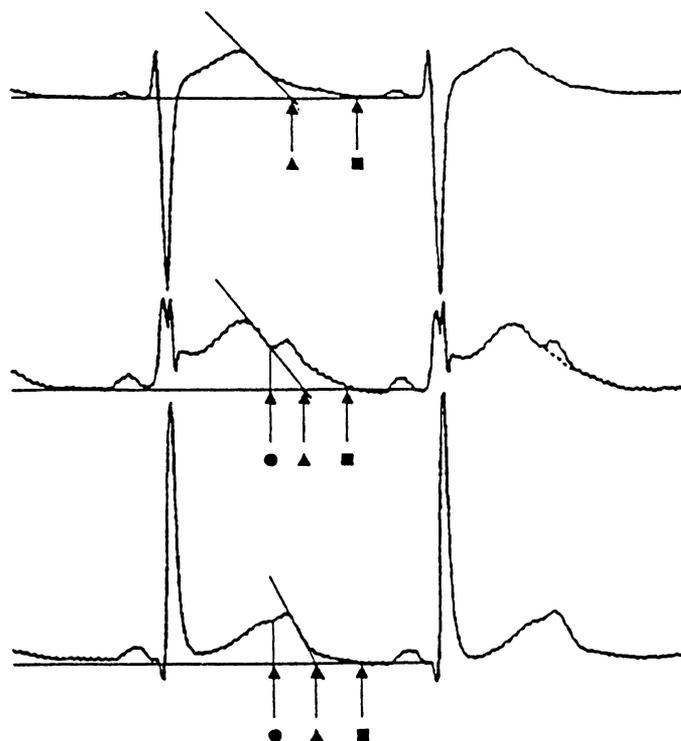


Figure 2.5: Different T wave end definitions 1.nadir between T wave and U waves 2. intersection of tangent line with baseline 3.return of polarization to isoelectric line

correlates poorly with that derived from QT intervals where the end of the QT interval is defined as the return of the T wave to the isoelectric line.

2.3 Clinical Value of QT Dispersion

Interpretation of results obtained from studies about QT Dispersion is not standardized in clinical practice since different methods are used. In some studies the clinical value of QTD will depend on its ability to predict arrhythmogenesis. In this thesis we have used the QTD to predict the ischemic heart disease (IHD). Remember that ischemia is a result of CAD. QTD increases reversibly during ischemia in patients with CAD. Ischemia occurs due to exercise or drugs such as dipyridamole and dobutamine [14]. Contrary to this, QTD decreases

such as dipyridamole and dobutamine [14]. Contrary to this, QTD decreases or remains constant during exercise in healthy subjects. During acute myocardial infarction QTD is very high in early days of infarction and decreases as reperfusion starts [15].

Liset N. et. al. [7] showed that the specificity of exercise ECG test for women increases up to % 100 if QTD is used as an additional diagnostic tool with ST analysis. They have measured the QT interval visually and used the standard definitions to form the QTD.

2.4 Exercise and Ventricular Repolarization

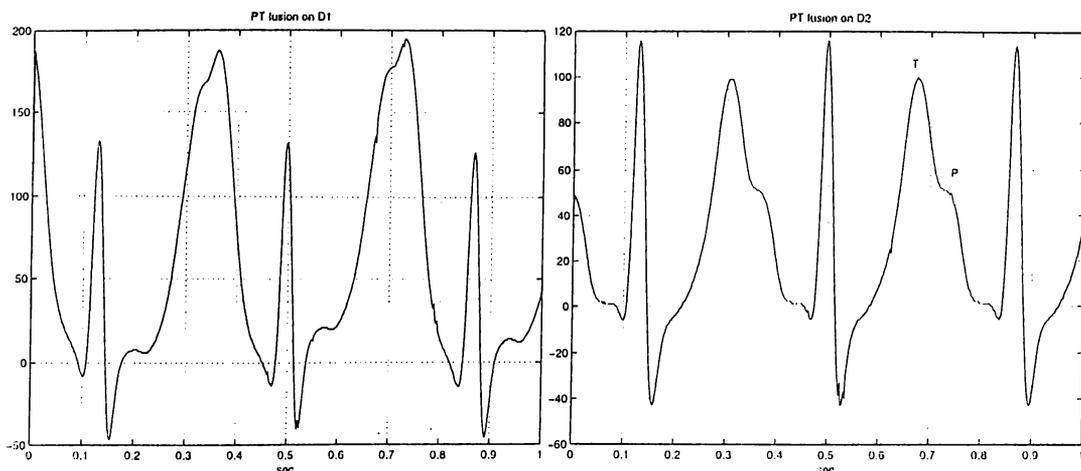


Figure 2.6: PT fused beats for leads D1 and D2

Exercise is a useful non-invasive method to produce variations in heart rate, causing dynamic changes in QTD. During exercise, dynamic parameters of the heart can be examined. It may cause arrhythmia and sudden death causing ischemia in patients with CAD. Measuring changes in QT interval (not QTD) during exercise was investigated to discriminate ischemic patients from nonischemic patients [16].

The exercise induced QT shortening depends on not only to the increase in heart rate but also on the level of catecholamine activity (such as adrenalin).

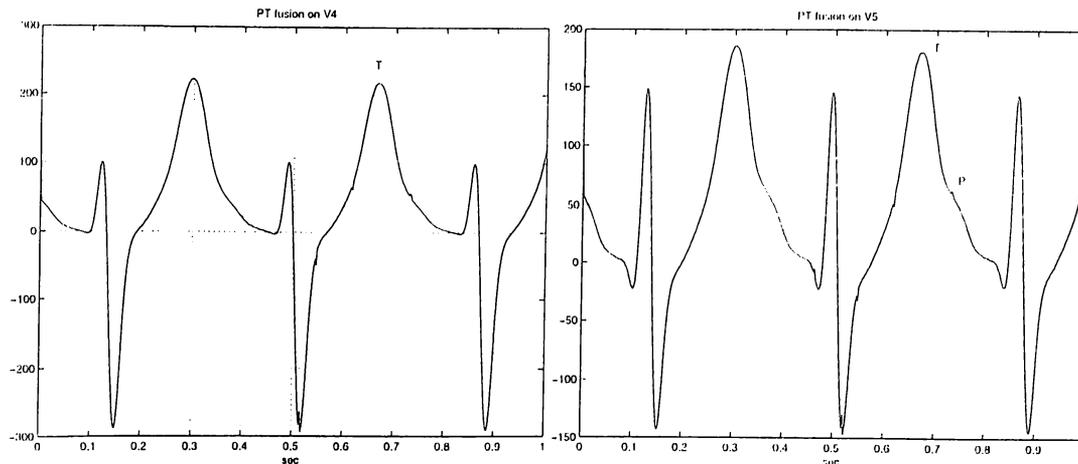


Figure 2.7: PT fused beats for leads V4 and V5

The response of ischemic myocardium to catecholamines in the blood is different than the non-ischemic myocardium which may cause the QT interval in ischemic myocardium to be longer. 12 lead ECG sees the different parts of the myocardium so the leads that are near to the ischemic myocardium will reveal a longer QT interval causing QTD to increase.

It has been shown that antiarrhythmic drug therapy (beta-blocker) and PTCA (an invasive method to reperfuse the ischemic myocardium) can decrease the QTD in ischemic patients during exercise [4].

Since the body needs more blood during exercise, the heart beats faster. As the heart rate increases a new depolarization of atriums occurs before all the ventricle muscles fully repolarized. This causes a PT fused beat and is one of the main problems while measuring the T wave end.

We can see T waves in some leads during exercise, which we do not see at rest, or some T waves can be lost during exercise. The morphology of T wave can change very much in some patients during exercise. In this case we need to update some of the algorithm parameters as the exercise progress.

Figures 2.6 and 2.7 shows the PT fused beats for D1,D2 and V4,V5. As seen in these figures the P wave of the beat at the right is under the T wave of the beat at the left. Thus it can not be seen.

Chapter 3

Methods

3.1 Data Acquisition

The electric field created by the heart propagates throughout the body and can be measured on its surface. The potentials are measured by placing electrodes to locations on the body. These signals are recorded as ECG data.

Exercise ECG test data recordings for this study were taken out in Ankara University, School of Medicine, Ibni Sina Hospital Cardiology Department. We have used a Kardiosis PC based exercise ECG system to record the data. 12 lead ECGs were recorded to harddisk during Bruce Protocol based exercise test with $500 \frac{\text{samples}}{\text{sec}}$ at 2.9 microvolt resolution. 89 exercise ECG test data are used for the study. The duration of the records vary from 5 Min. to 20 Min. The complete block diagram of the algorithm is shown in figure 3.1.

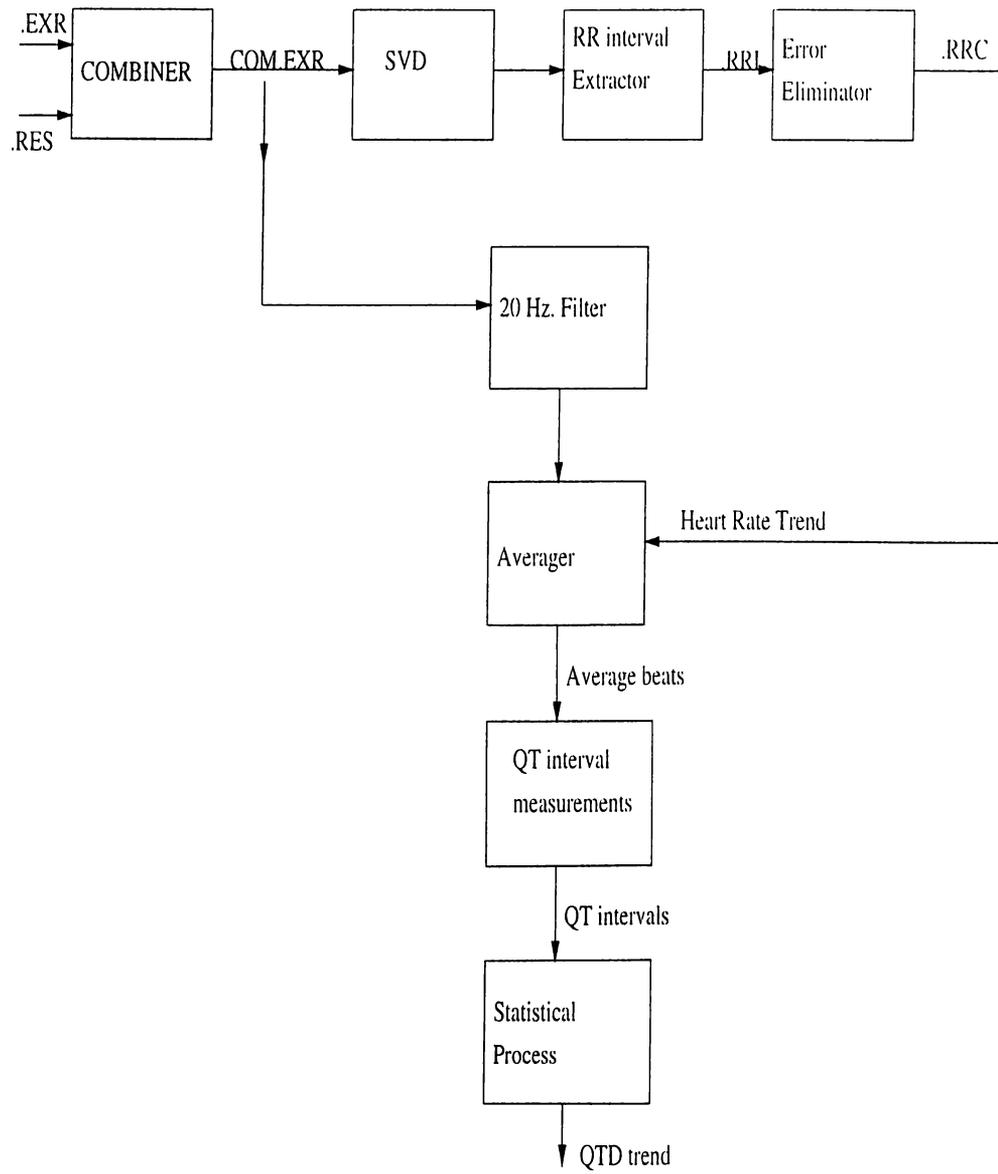


Figure 3.1: Block Diagram of the algorithm

3.2 Obtaining Heart Rate Trend

QT interval measurements have been done on time averaged ECG complexes. In order to obtain the time averaged ECG complexes we need the heart rate trend. We have to know the places of the R waves on the record exactly. R wave was chosen as the alignment point for averaging since it is easier to detect. Also we will use this information to investigate the relation between QT interval and heart rate trend.

Recorded data files during exercise have the extension of .EXR. 73 characters from the beginning of these EXR files contain the information about the subject. Following 73 characters, standard 12 lead ECG record is found. Leads are recorded one after another using 2 byte integers for each sample. Also a 30 second rest ECG data is recorded with the extension .RES when the patient is standing. We have recorded these raw data to CD-ROM for future usage.

RR interval tachograms are extracted by identifying the R waves through the record. We make this identification using a template-matching algorithm. This algorithm is based on calculation of Cross Correlation Coefficient (CCC) between the composite ECG signal and a template produced from the ECG signal.

3.2.1 Recognition of QRS Complexes

The rest and exercise ECGs are combined and a file with the extension COM.EXR is obtained. The first 30 sec of this file is the rest ECG and the remaining part is the exercise ECG. We process the combined data using an online SVD algorithm to obtain 2 orthogonal channels [17]. This process filters the EMG and baseline noise. We have applied first orthogonal component of the output of the SVD algorithm to QRS recognition program. The first orthogonal component carries most of the energy in the ECG the others carry the noise energy. The first orthogonal component is referred as composite ECG.

QRS complex recognition begins with detecting R waves on composite ECG

by the help of a simple method. This has been done using a threshold algorithm. Since the steepest change on surface ECG occurs at R waves, it is enough to detect the high slope of the R wave. First the signal is filtered with a digital filter with difference equation shown in equation 3.1.

$$Y_f(n) = X(n + 9) - X(n - 1) \quad (3.1)$$

where X is the input signal. This filter removes baseline variations, high frequency EMG noise and cancels the effect of 50 Hz. We detect the R waves roughly using a slope threshold algorithm. A template beat is obtained from the beginning of this filtered composite ECG signal [18] by averaging 4 to 8 beats. The points to coincide these beats are found by threshold algorithm.

Recognition of R waves throughout the exercise ECG is done by matching the template with the data. The CCC between the data and predetermined template is calculated for precise matching. We need a very precise matching for time averaging. The CCC calculations take considerable time, due to divisions and multiplications involved. In order to reduce the computation time, CCC calculations have not been done on every point through the data. The locations of the R waves are detected roughly initially by comparing the derivative signal with a threshold value determined in the template creation stage. The threshold value is taken to be %70 of maximum derivative of the template. When the R wave is detected roughly using a threshold, to locate it precisely, CCC calculations are performed for 50 points around the initial detection point. We use the formula in equation 3.2 for CCC calculations.

$$CCC(m) = \frac{\sum_{i=-24}^{35} x(n + i + m).T(i)}{\sqrt{\sum_{i=-24}^{35} x^2(n + i + m). \sum_{i=-24}^{35} T^2(i)}} \quad (3.2)$$

where x is data, T is the template, n is sampling instant, i is the index of summation, m is the shift around the alignment point. The point at which CCC reaches its peak is defined as the alignment point for that R wave. Also CCC must be greater than 0.8 to accept this beat.

As the exercise progresses QRS morphology changes, after a time the initially chosen template loses its correlation with the data. Thus the template is adapted to newly coming data. The template at that instant is averaged with

the accepted beat and this averaged signal is denoted as the new template. This algorithm has been implemented using Borland Pascal for the PC. The output of this program is the location of the beats in the file with the extension COM.EXR . The extension of output file is .RRL .

Although this program uses many precautions for correct detection of R waves, it sometimes misses the beats or classify the T wave as the QRS complex depending on the derivative threshold chosen at the beginning. Thus a correction of these errors is needed. If we plot the RR interval the spikes can be seen which are created by the detection errors in Figure 3.2. The spikes between beats 0-200 and 1000-1100 are corrected by a MATLAB program.

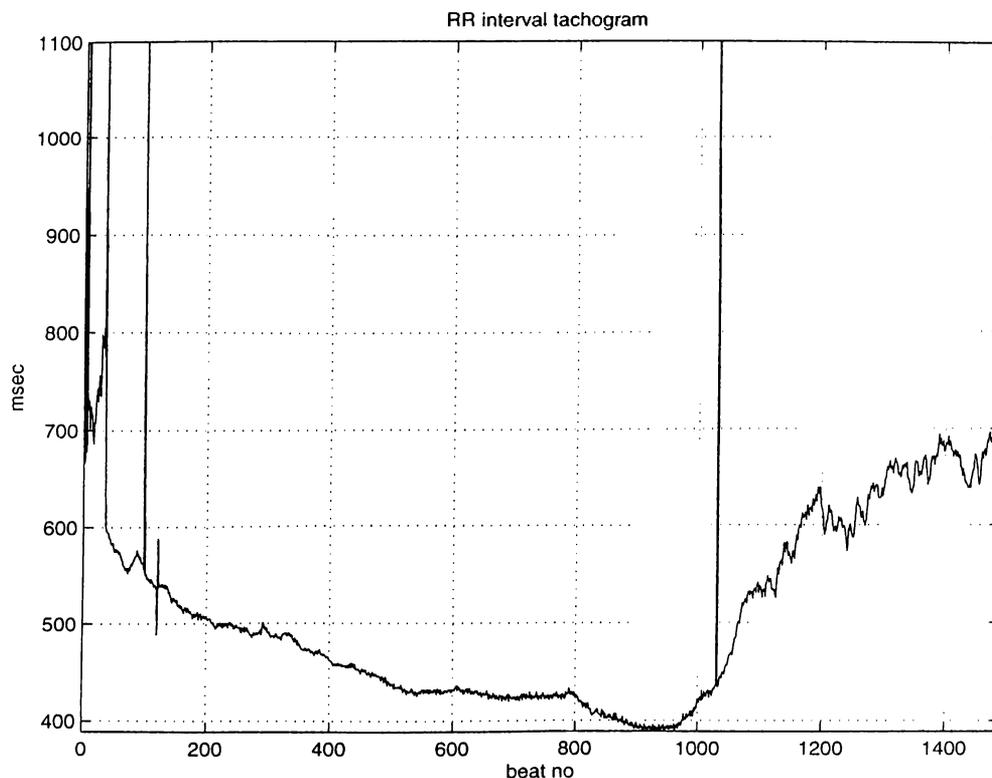


Figure 3.2: RR tachogram showing the detection errors

These detection errors are detected using a program that takes the derivative of RR tachogram and rejects the beats leading a high derivative. These beats are not included in the following averaging process since they are doubtful. But in order to see a RR tachogram without spikes the RR interval causing the spike is placed by the mean of previous and next RR intervals. The outputs of the correcting MATLAB program are the files with the extension .RRC .

3.3 Obtaining the Average Beats

After having the places of alignment points (R wave) during the exercise record we can obtain the average beats from the raw data. We use the raw ECG data (COM.EXR files) to obtain the average beats using the information of RR intervals.

3.3.1 Filtering

The first step of the averaging is filtering the input raw data with 20 Hz. low pass filter (LPF). Since RR tachogram is obtained previously from a different signal (SVD orthogonal component), we need a zero-phase 20 Hz. LPF filter in this step. Otherwise, the alignment point found previously using composite signal does not coincide with raw data's R wave. If the alignment point of the beats shift, the signal is lost at the averager output. The implementation of this filter should be fast since we want to use this algorithm in real time.

We input the noisy signal through 4 cascaded averaging filters. Since the operation in this filter is only averaging, no phase shift is introduced and it is easy to implement. Figure 3.3 and Figure 3.4 shows the block diagram and frequency response of this filter respectively.

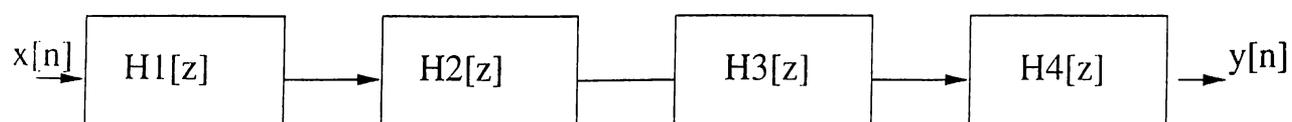


Figure 3.3: 20 Hz filter block diagram

$$H_1(z) = \frac{1}{10}(z^{-1} + z^{-2} + \dots + z^{-10}) \quad (3.3)$$

$$H_2(z) = \frac{1}{9}(z^{-1} + z^{-2} + \dots + z^{-9}) \quad (3.4)$$

$$H_3(z) = \frac{1}{7}(z^{-1} + z^{-2} + \dots + z^{-7}) \quad (3.5)$$

$$H_1(z) = \frac{1}{6}(z^{-1} + z^{-2} + \dots + z^{-6}) \quad (3.6)$$

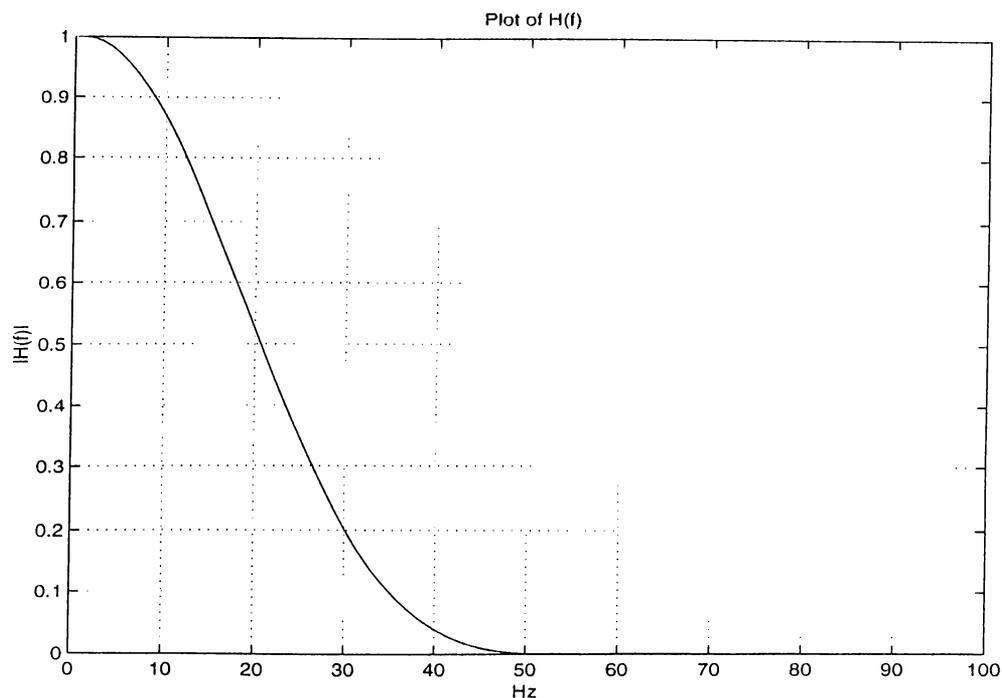


Figure 3.4: 20 Hz filter frequency response

The 3 dB cut-off frequency of this filter is approximately 16 Hz. The filter removes the EMG noise (high frequency) without effecting the T wave morphology since T wave is low frequency.

3.3.2 Averaging the Beats

Once the places of the R waves are determined and the signal is filtered we can obtain the average beats for 8 channels. The remaining 4 channels are obtained from the linear combination of other channels after averaging.

The averaging has been done for 10 sec. of record. For each 10 sec. of data, one average beat is obtained. We count the number of beats in 10 sec. record slice using the previously determined RR interval tachogram. The beats that are in that 10 sec. slice are added by aligning R waves (predetermined

alignment point) and the summation is divided by the number of beats added. As a result the average beat is obtained. The eliminated doubtful beats during correction of RR tachogram are not added in this average beat. The noise level decreases since it is random noise signal. If the alignment point for each beat shifts during averaging, a low pass filter effect is observed and the signal is lost. That is the reason why we have to detect the R waves very precisely. The average beat's SNR is higher than one beat's SNR.

The duration of the average beat is 1 sec. For high heart rates the time interval between the beats shorten. If the RR interval is less than 0.5 sec., we see 3 beats in 1 sec. record. But the beat whose parameters we will measure is the one in the middle since the alignment is done with respect to that beat. This beat is referred as the main average beat (MAB). The alignment point is approximately the 250th sample in 1 sec. record. We repeat this process for 8 channels. For a record of 1200 sec. long we will obtain 120 average beat per channel. Each average beat's duration is 1 sec. long. Figure 3.5 and 3.6 shows two average beats obtained during rest and exercise respectively. A high PT fusion is observed in Figure 3.6.

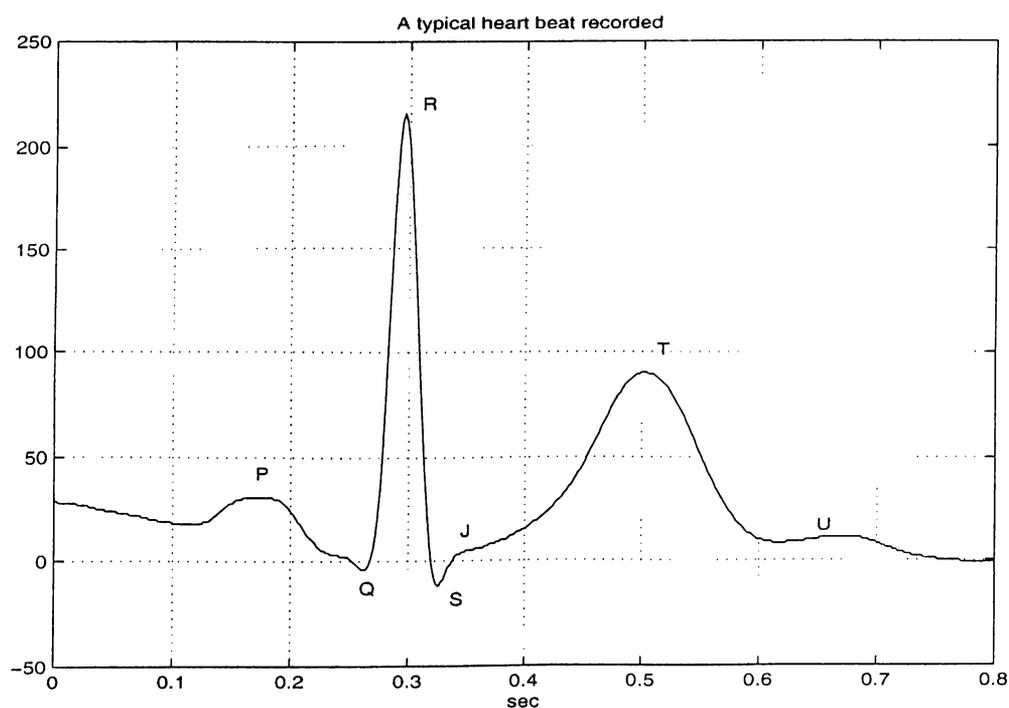


Figure 3.5: Average beat at rest

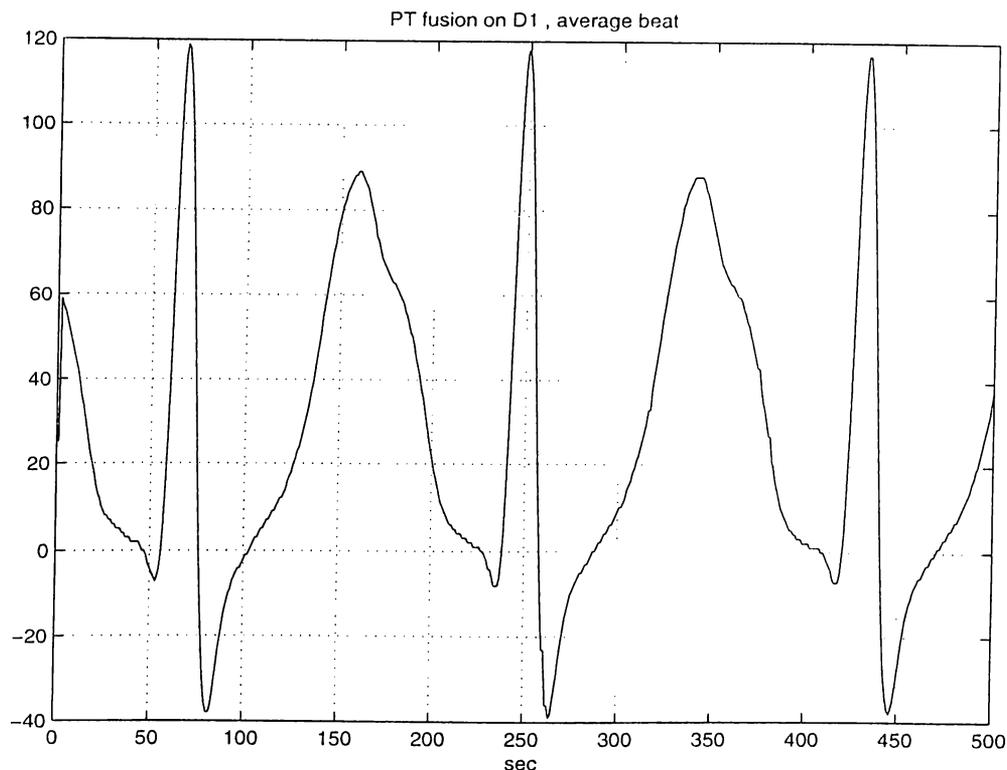


Figure 3.6: Average beat at peak exercise

Although we remove the high frequency noise using 20 Hz. LPF, this filter can not remove the baseline noise since it is a very low frequency signal. If one or more beats included in the average beat has a great baseline variation, this effects the average beat morphology very much. In order to remove the baseline variation in the MAB, a baseline correction has been done, as described below.

Initially, the beginning the end of the MAB has been detected roughly using a simple derivative search algorithm. These points are called V_a and V_b respectively. For a baseline free beat the voltage levels of these points must have the same voltage level. The mean voltage levels of these two points were obtained by averaging 5 points around the V_a and V_b . We calculate the equation of the line passing through V_a and V_b . This line has been subtracted from the average beat to correct the baseline variation. If there is no baseline variation this line has a slope of 0. Figure 3.7 shows baseline noise on the beat (original) the line modelling this baseline noise and baseline corrected beat. The beat varies around 0 voltage level after correcting.

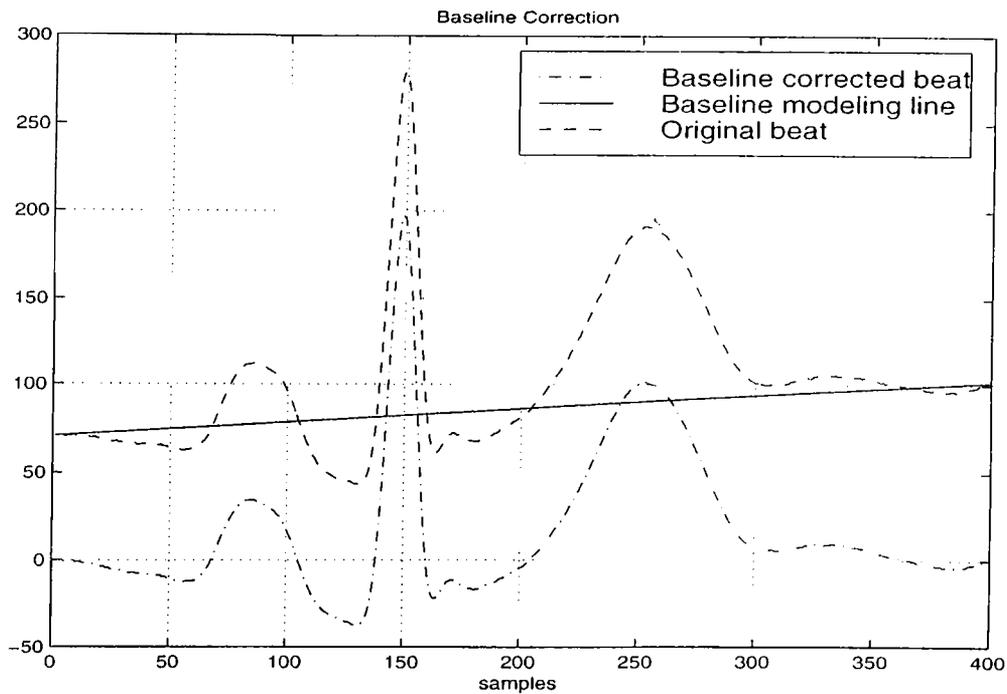


Figure 3.7: Baseline Correction of the beat

As a result of averaging and baseline correction a clean beat has been obtained on which we can measure the QT parameters more accurately. The output of this program is the file with the extension .TEF. In these files, average beats for 12 channels, mean RR interval for 10 sec. record and the number of beats included in the average beat are written.

3.4 Measuring the Parameters

After obtaining the clean average beat we can detect the fiducial points and measure the necessary parameters for QT interval measurement. All the measurements after this point have been done on the MAB.

3.4.1 Detecting the Q Point and T Peak

The first step when measuring the QT interval is detecting the Q point. Also the T peak should be detected correctly which will give us a clue to detect the T wave end in the future calculations. We obtain the derivative of the average beat since it is less sensitive to noise using equation 3.7. Figure 3.8 shows the beat and its derivative found using that equation.

$$d(n) = \frac{x(n) - x(n - 2)}{2} \quad (3.7)$$

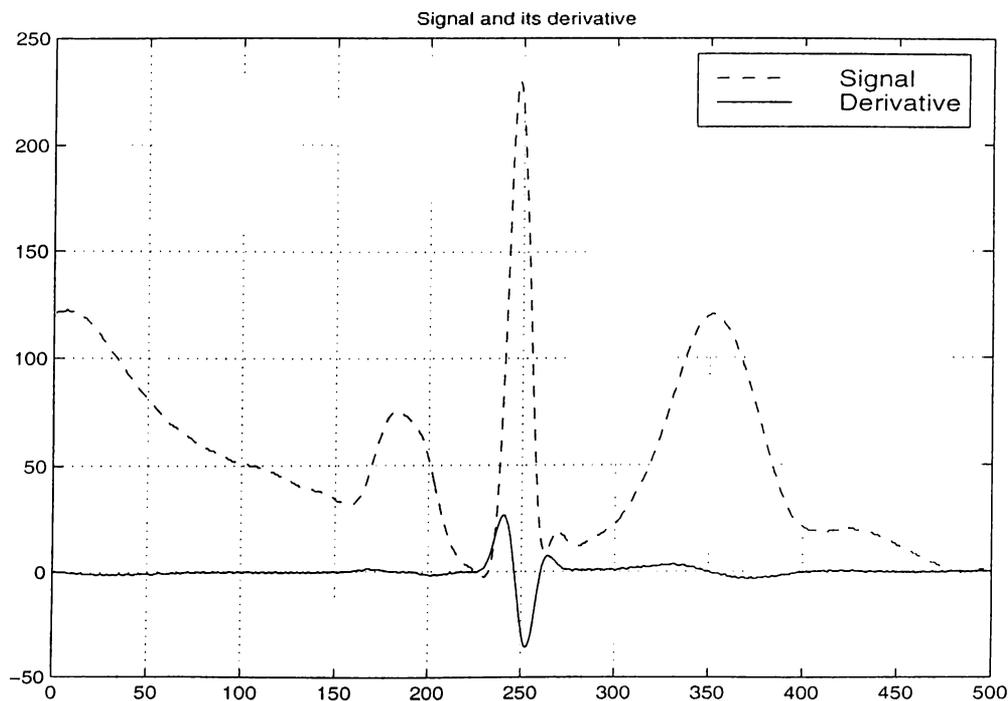


Figure 3.8: The average beat and its derivative

The 250th sample is in the middle of the average beat and it is approximately somewhere on the increasing edge of the R wave. We know that Q point always precedes that alignment point (R wave). Q wave is near to R wave so starting to search the Q point 50 ms. before the R wave would be a good choice. Defining a Q point search window also reduces the time to search it. We search the Q point between samples 225 and 250.

Q point is detected searching the first point (starting from the 225th sample)

for which $d(n) \geq 1$. This has been done for 12 channels separately. We will measure all the voltage levels for other fiducial points with respect to baseline voltage level. Hence we need to calculate the baseline voltage level. Baseline voltage level is calculated as the mean value of 10 points before Q point. The calculated baseline voltage level is approximately zero since we have corrected the baseline previously. In spite of this, we calculate it again in order to obtain more precise measurements.

The duration of QRS complex can not be larger than 100 ms even in worst case conditions. If we divide the QRS complex into two equal parts, R wave being in the middle, most probably after 50 ms from R wave QRS complex will end. Thus the J point search window is defined between samples 250 and 275. The J point is defined as the point where the QRS complex returns to baseline. The J point is detected in a similar way to Q point detection. The first point where $d(n)$ exceeds 3 in a window of $250 < n < 275$ was referred as J point. J point will give us the point to start searching the T peak since it is the end of the QRS complex. Also ST60 and ST80 measurements can be done easily when we detect this point.

Detecting the T wave peak is the most challenging measurement since we have numerous T wave morphologies. Figure 3.9 shows these morphologies [1].

Arrows in each panel indicate the major features of each complex.

- A.) Early repolarization (J-point elevation), normal variant.
- B.) Acute pericarditis: (1) depressed T_a ; (2) elevated ST (3) normal T.
- C.) Early Acute Myocardial Infarction (AMI): (1) Elevated ST; (2) tall, peaked T wave; steep angle between 1 and 2.
- D.) AMI (1) small Q wave (2) elevated ST segment ; (3) tall, peaked T wave with steep angle 2 to 3
- E.) AMI: (1) pathologic Q wave; (2) elevated ST segment; (3) terminal T wave inversion.
- G.) Angina pectoris with ST elevation during pain.
- H. and I.) Angina pectoris with horizontal or downward sloping ST segment during pain or exercise.
- J.) j-point depression with upsloping ST segment during exercise, normal response.
- K.) Primary T wave inversion (2) in ischemia or primary muscle disease.

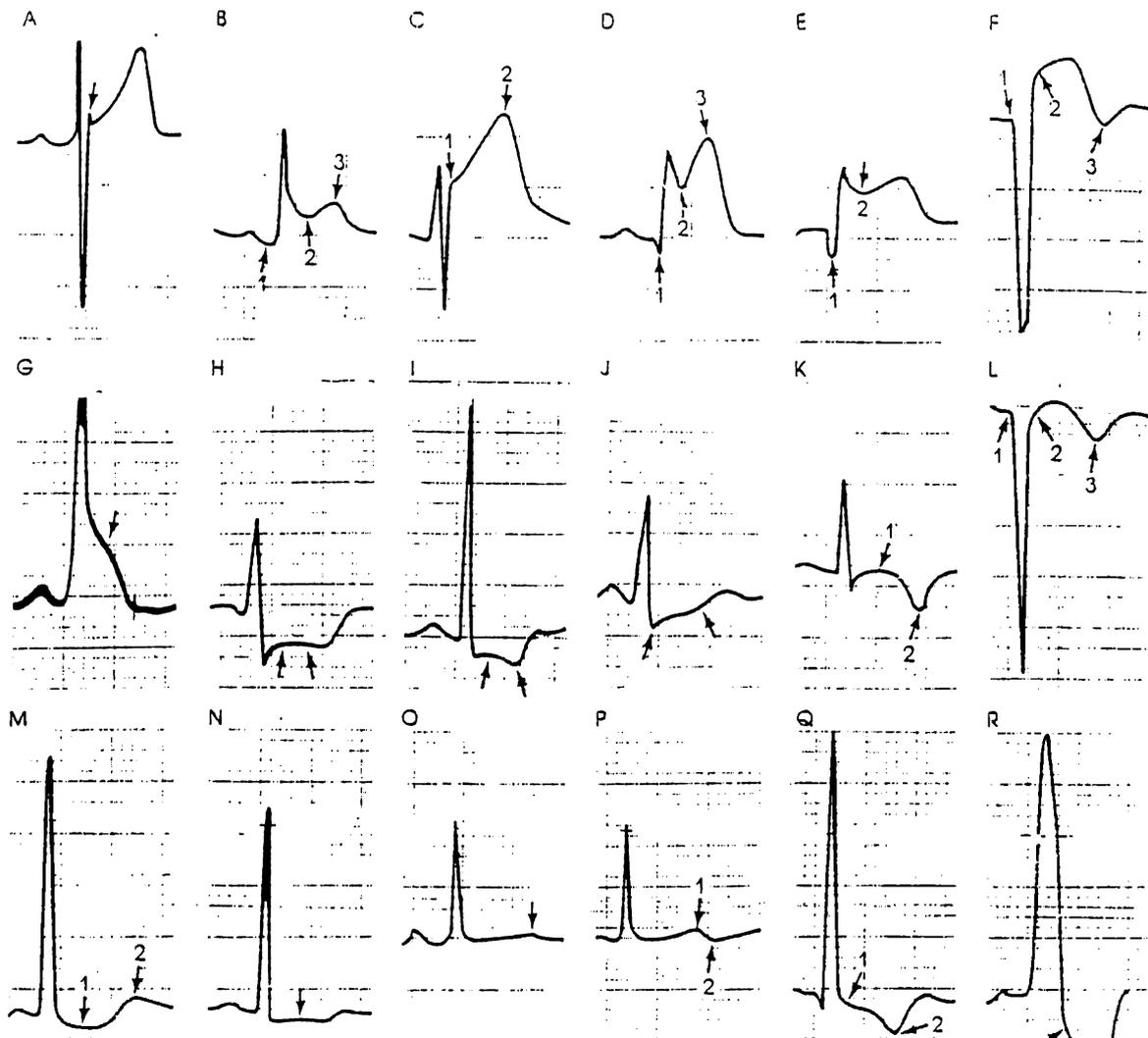


Figure 3.9: Various T wave morphologies [1],

L.) Myocardial infarction (healed): (1) pathologic Q; (2) ST returning to baseline; (3) symmetrically inverted T wave

M.) Digitalis effect: (1) downward coving of ST segment, merging into an upright T wave.

N. to P.) Non-specific ST segment and T wave changes often seen in chronic ischemic heart disease.

Q.) Left ventricular strain pattern with (1) downsloping ST segment and (2) asymmetrically inverted T wave.

R.) Downsloping ST segment merging into a deeply inverted T wave in ventricular conduction abnormality.

Due to these abnormalities it is difficult to find a unique algorithm for all types of T waves. In the figures N, O and P the amplitude of T wave is very low. In the others we can not define the T peak very easily. Also due to PT fusion at very high heart rates, P wave peak can be detected as T wave peak which causes great errors in the measurements. An easy and effective algorithm is suggested to find the T peak and T end in this study. The most important measurement in this study is detecting T peak and T end.

A second generic baseline referred as baseline2 is calculated as the mean of 15 points after $J_{point} + 20ms$. At that point it is guaranteed that QRS complex ends and returns to baseline. This point is either elevated or depressed with respect to baseline at patients who have ischemia. The T peak is searched with respect to baseline2 that gives the best results for depressed, elevated ST segments, biphasic or strange T waves as shown in figure 3.9.

T wave peak is defined as the absolute maximum point on the ECG itself with respect to baseline2 in a predefined window. The definition of that window is very important in the detection process of the T wave peak. If we select the window too narrow we can not reach the T wave peak while searching. On the other hand, if it is too wide the P wave peak at the right of the MAB can be detected as T peak if its amplitude is larger than T peak.

As the heart rate increases, the T peak approaches to QRS complex and the P wave of the following beat fuses to T wave. So the window size should be changing with respect to heart rate. As the heart rate increases window size should be smaller and vice-versa.

Figure 3.10 shows the T wave peak window definition for a PT fused beat. The end of the window is just between the T peak and the PT fusion point in this figure.

It is a physical fact that T wave is always after the J point and not before the $J_{point} + 80ms$. $ST80$ measurement is used by cardiologists for diagnosing the exercise ECG test. $ST80$ measurement is the voltage level of the point, $J_{point} + 80ms$, with respect to baseline. Thus it is verified that T peak can not

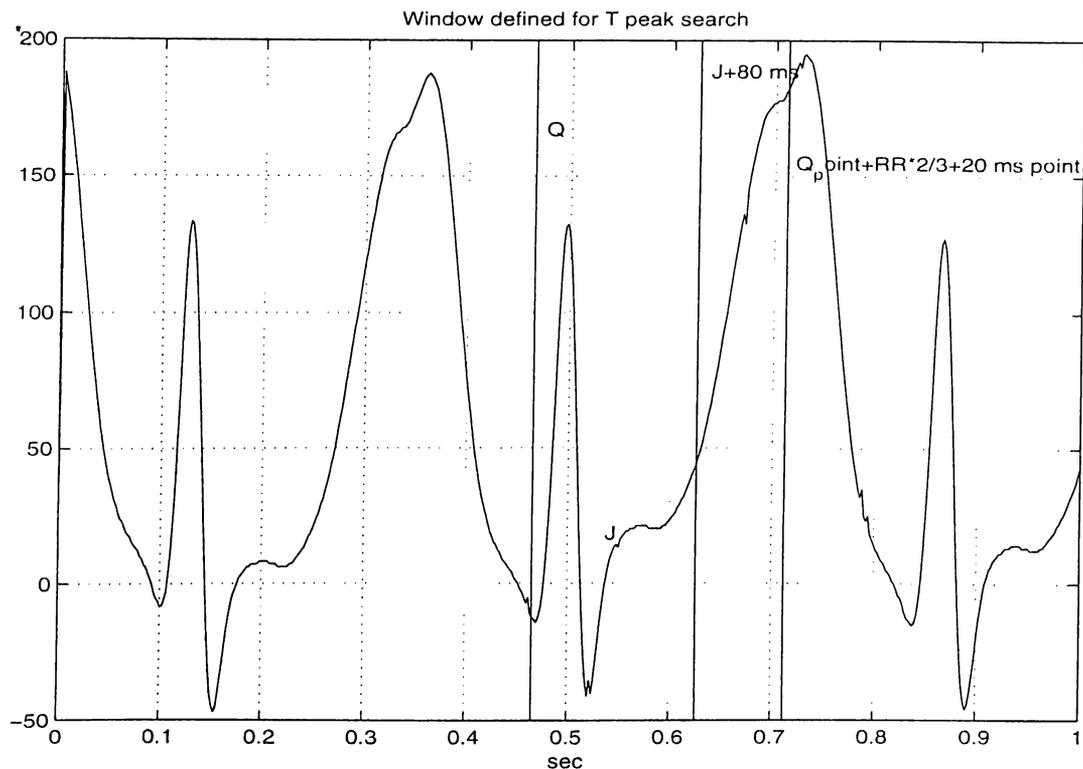


Figure 3.10: T wave peak search window

occur before $J_{point} + 80ms$. It will be a good choice to start searching T peak from $J_{point} + 80ms$.

The point $Q_{point} + RR_{int}$ defines the Q_{point} of the beat at the right. It is again a physical fact that T peak is before that defined point. If we divide the time between two consecutive Q points into 3 slice the PT fusion during exercise mostly occurs in the last slice. Thus the T wave peak search ends before $\frac{2}{3}$ of RR_{int} (considering a tolerance) in order to cope with PT fusion artefacts. In order to not to get the P wave of the beat at the right, the T wave peak search window can be defined as:

$$J_{point} + 80ms < t < (Q_{point} + RR_{int} * \frac{2}{3} + 20ms) \quad (3.8)$$

The 20 ms is a tolerance value and can be decreased if very high PT fusion occurs or increased if T peak occurs very late. If we detect the T wave peak exactly it is guaranteed to measure the T wave end. The T wave amplitude

measured with respect to baseline voltage level is kept for 12 channels in an array to use it for the elimination of wrong measurements.

3.5 Detecting the T wave end

For years the T wave end is detected by cardiologists visually, using a simple algorithm. They used rulers, pencils and magnifier glasses for that purposes. This was a very difficult, boring and time consuming procedure. They fitted a line to the falling side of the T wave. They have referred this line as the tangential line to falling edge of T wave. The intersection of this line with the baseline voltage level is defined as the T wave end. This has been shown in Figure 3.11.

This method is verified by the researchers and is the main idea of this study to detect the T wave end. Some modifications and additions have been made to this procedure to make it more efficient and to implement it using a computer.

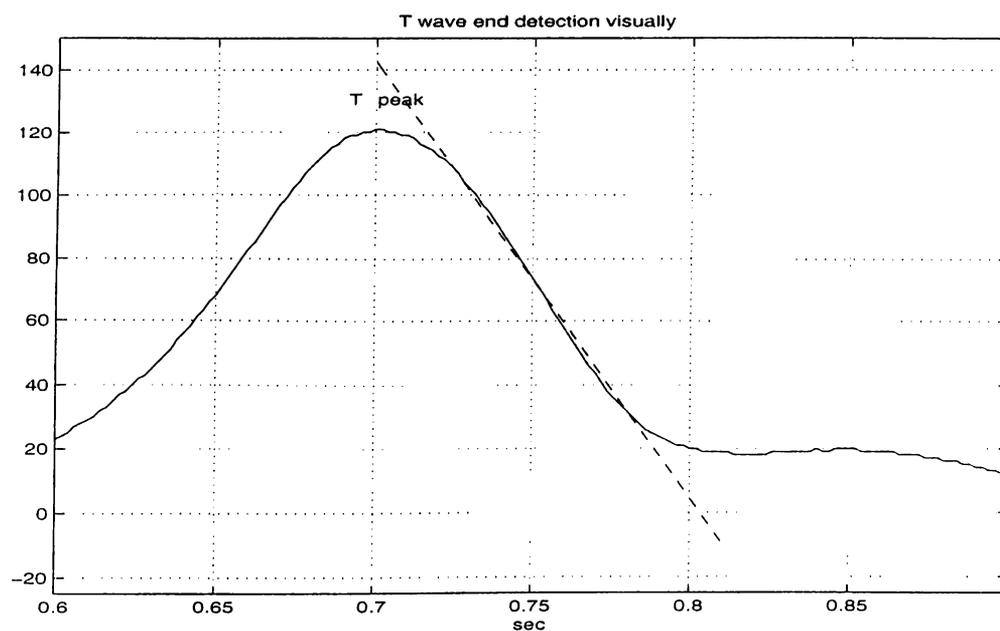


Figure 3.11: The T wave end detection visually

Although using the ruler and pencil method gives good results, implementing it to a computer may reveal erroneous results due to noise or PT fusion. The points to fit the tangential line are very difficult to detect in exercise ECG. If the T wave's amplitude is too low the slope of the line approaches to 0 and the intersection with the baseline does not occur. So a pre-processing is necessary before finding the tangential line.

This pre-processing is achieved by fitting a 2^{nd} degree parabola to the points in the window of $T_{peak} - 52ms < t < T_{peak} + 64ms$ by Least Squares Approximation technique. This window is found empirically. Window may contain the PT fusion point but this does not effect the fitted parabola since it models the whole T wave peak. The equation of the parabola is shown in equation 3.9. We obtain the coefficients **a**, **b** and **c** of the 2^{nd} degree parabola.

$$y(t) = a * t^2 + b * t + c \quad (3.9)$$

In order to fit a second-degree parabola we have to solve the equation system 3.10. This equation system is obtained when the derivative of the length of error vector between the estimated and real signal is equated to zero. In other words we must minimize $S = \sum_{i=1} (y_i - c - bx_i - ax_i^2)^2$ with respect to **a**, **b** and **c**.

$$\begin{bmatrix} n & \sum x_i & \sum x_i^2 \\ \sum x_i & \sum x_i^2 & \sum x_i^3 \\ \sum x_i^2 & \sum x_i^3 & \sum x_i^4 \end{bmatrix} \begin{bmatrix} c \\ b \\ a \end{bmatrix} = \begin{bmatrix} \sum y_i \\ \sum y_i x_i \\ \sum y_i x_i^2 \end{bmatrix} \quad (3.10)$$

X_i goes from $T_{peak} - 26points$ to $T_{peak} + 32points$ ($i = 0 \dots 58$) . y is the array of data to fit the parabola.

The *conjugate gradient* algorithm is used to solve this linear system of equations. It is very fast and gives very accurate results. Its complexity is $O(n)$ where $n=3$ in this system of equation.

This process is immune to noise, small spikes in T wave, PT junction or strange T wave morphologies since it is trying to fit a parabola to 58 points

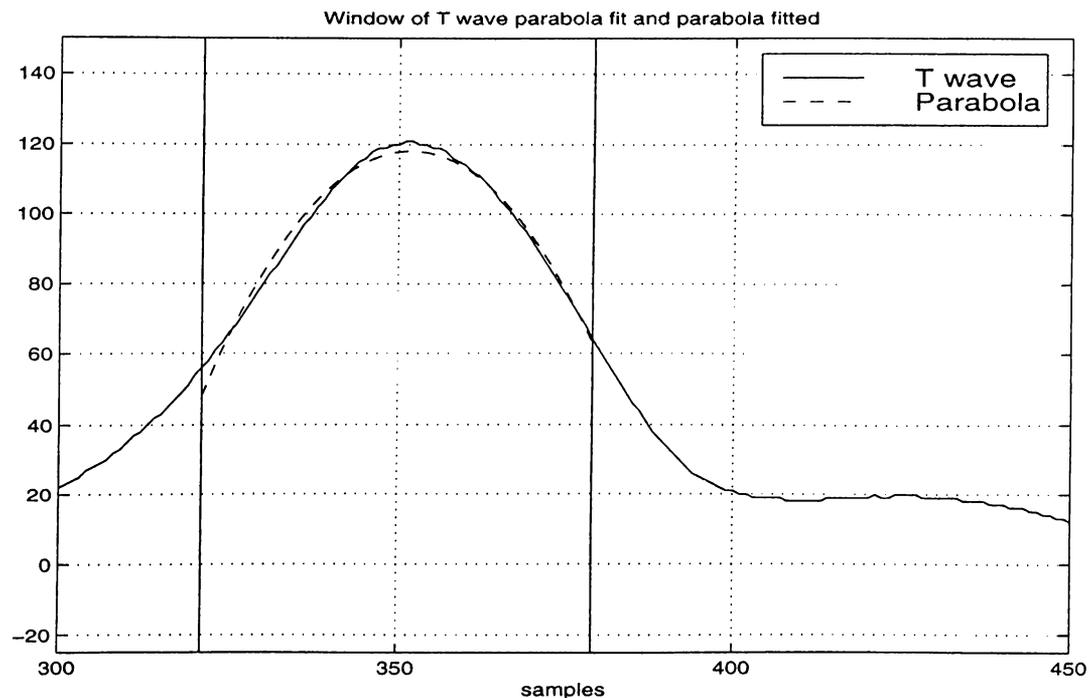


Figure 3.12: The window of parabola fit and parabola fitted to T wave peak

around T peak. It is not looking at only falling edge of T wave as the previous studies or medical doctors do. As seen in Figure 3.12 T wave peak can be modeled with a parabola easily.

The intersection of the right arm of the parabola with the baseline voltage level could be referred as the T wave end. However this method detects the T wave end at the left of the exact T wave end since the right edge of the T wave can not be modelled with this parabola. It can be modelled by a line as the cardiologists do.

Modelling the T wave peak with the parabola gives us the opportunity to find the point to fit the tangential line very easily since the parabola is noise free unlike the ECG itself. The peak of the parabola is found easily. After finding the value of the peak of the parabola and its location we search the point, where the parabola takes the % 80 of its absolute maximum, on the right arm of the parabola. We refer this point as the V_{80} point. The parabola has a slope at that point (M_p). A tangential line to the parabola at V_{80} with the slope M_p is calculated. That is the line which is found by the cardiologists

visually. The intersection of the tangential line with the baseline voltage level is referred as the T wave end. Figure 3.13 shows the parabola, fitted line.

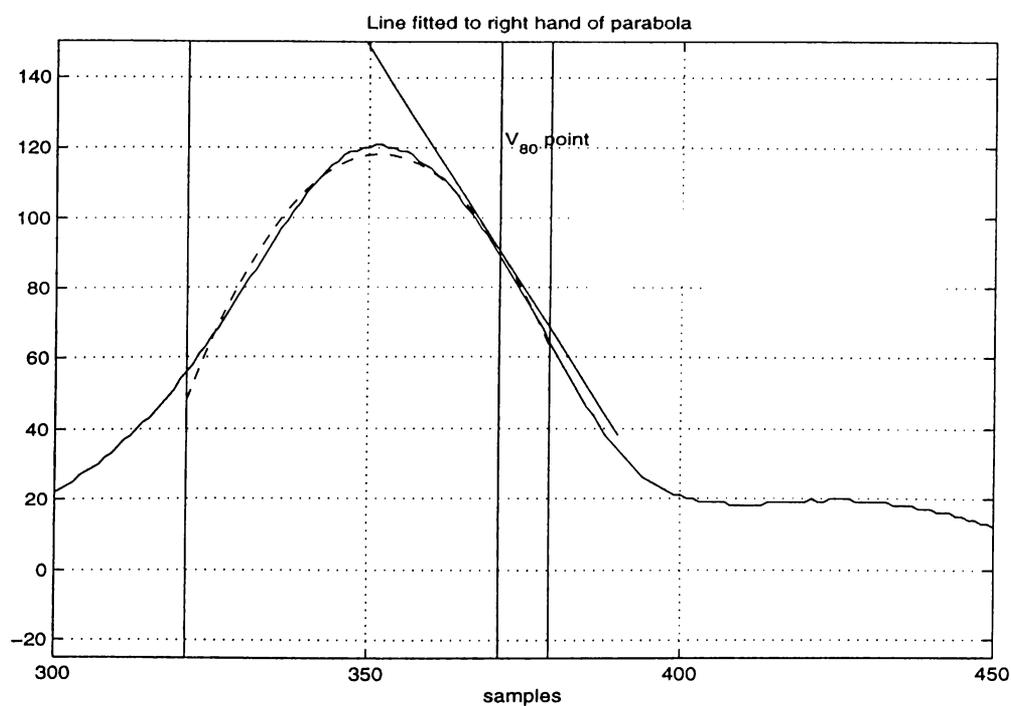


Figure 3.13: The parabola window, parabola and tangential line

Figure 3.14 shows the parabola and line fitting process for a PT fused beat. As seen although the PT fusion point is inside the parabola fitting window it does not effect the shape of the parabola very much. Thus T wave end is detected correctly.

This method can detect the T wave end even there is a PT fusion since the 2nd degree parabola can not model this junction. The algorithm is visually verified that it detects the T wave end accurately by viewing the signals for 70000 beats.

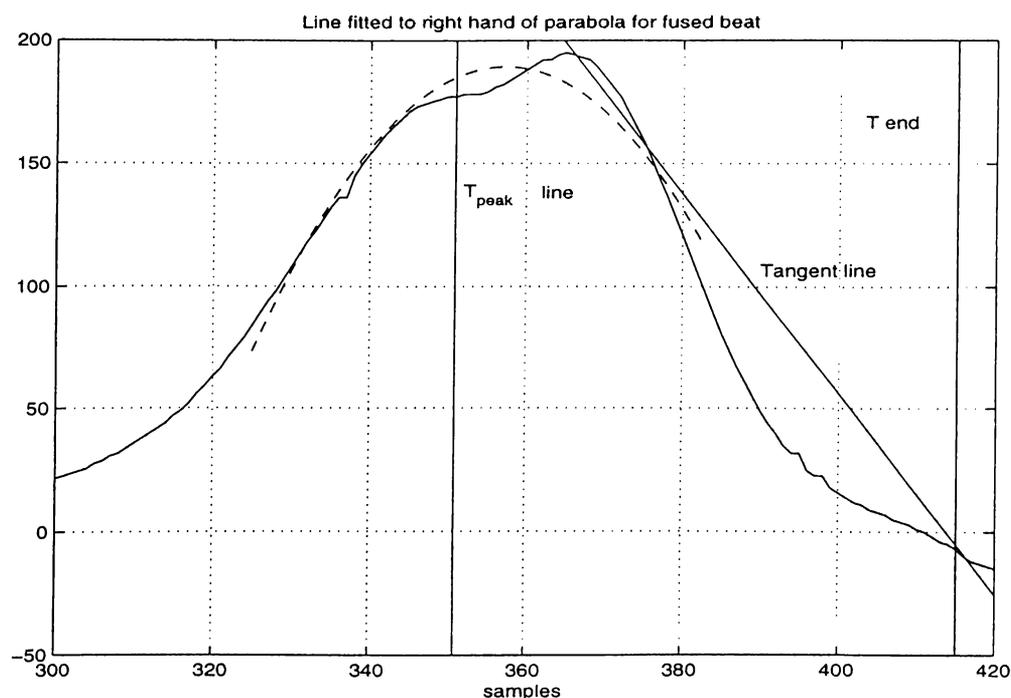


Figure 3.14: The parabola window, parabola and tangential line for PT fused beat

3.6 Checks for Eliminating the T Waves and Measurements

Although T wave end detection algorithm is designed to cope with the artefacts that occur during exercise, we eliminate the beats that can give erroneous results. -1 is written to the output file for unmeasured beat parameters. Sub-sections 3.6.1 and 3.6.2 defines the pre-measurement checks since these checks are done before parameter measurement.

3.6.1 Cross Correlation Coefficient Check,(CCCC)

Since the CCC check is done during RR tachogram extraction process on the output of SVD algorithm the raw signal is not checked for great noise or shape distortions. Although we filter the signal using a 20 Hz. filter, a great amount

of noise can effect the average beat very much during exercise. When this situation occurs, no ECG like signal is seen in the average beat. The average beat is only a lot of noise. Thus we have to check if the signal is like an ECG or noise before starting the measurements.

This has been achieved by calculating the CCC, between the current QRS complex on which the measurements will be done and the template QRS complex. The QRS complex template is actually the QRS complex taken from rest ECG record. If the $CCC < 0.75$ then no measurement is done on that beat for all leads. This means that this beat is not like an ECG signal. We assume that, if QRS complex is corrupted with great noise T wave is already corrupted with noise.

3.6.2 Amplitude, PT Fusion and Energy Checks

If the beat passes the CCC Check, Q point, J point and T wave peak detection have been done but we still need to check the T wave morphology. If the amplitude of the T wave is very low or there exists a high PT junction it is hard to measure the T wave end. If we can measure it, with a high probability the measurements will be wrong. For example, if the T wave amplitude is very low the tangential line does not intersect the baseline. Thus before measuring the T wave parameters we should check if T wave has high amplitude and it is not a noise spike.

If the T wave amplitude is greater than 0.1289 mv., T wave passes amplitude check. This amplitude threshold is an important parameter during measurement and can be decreased for the patients who have low T wave amplitudes.

If there is a spiky random noise the T wave can pass the amplitude check because of that spike. If the rest of the T wave has still low amplitude, a tangential line can not be found. Thus a spike and random noise check should be done.

The energy of the T wave is calculated by adding the amplitudes in a

window of $T_{peak} - 60ms < t < T_{peak} + 60ms$. The energy is low if there is a small amplitude random noise on low amplitude T wave or a spike occurs instead of a real T wave. If energy is greater than 4.684 mv. the T wave passes the energy check. This limit could be changed but it was a good choice for that study.

As the last step we check if there is a highly fused P and T waves and the T wave is suitable to fit a second-degree parabola. These tests are necessary since we can have strange T wave morphologies. It is better not to measure these T waves instead of measuring and having erroneous results.

If the absolute voltage difference between the T peak and the both corners of parabola fitting window ($T_{peak} - 52ms < t, T_{peak} + 64ms$) exceeds 0.0435 mv. at the same time the beat passes the last pre-measurement test. This checks if the T wave peak can be modelled with a parabola or not.

3.6.3 Post-measurement Checks

If the beat passes the pre-measurement tests a second-degree parabola is fitted to the peak of the T wave as described in the sections above. After the parabola fitting process, the coefficients of the second degree parabola (a,b,c) are checked to see if the T wave is very flat or not.

If $abs(a) > 0.001$ or $abs(b) \geq 0.7$ the wave passes the post-measurement test and T wave end is detected. The tangential line is calculated. If a is very small in amplitude then the T wave is very flat. As seen in Equation 3.9 as a approaches to zero $y(t)$ approaches to a line.

After T wave flatness test we check the measured T wave end parameters to see if they are suitable to physical facts. T wave end can not be larger than 1 sec. since the length of the average beat is 1sec. If $T_{end-time} > 980ms$ (remember that each average beat is 1 sec. long) the measured T wave end is excluded.

As a physical fact, T wave end can not occur before T peak. Thus if $T_{end-time} < T_{peak-time} + 20ms$ this measurement is excluded too. T wave end

can not occur after the Q point of consecutive beat. Thus if $T_{end-time} > Q_{time} + RR_{interval}$ the measured T wave end is excluded. These checks are called post-measurement checks since we check the parameters after measuring them.

These checks have been done for each lead and an array of length 12 is filled with QT interval data.

After measuring the QT interval for 12 or less leads we find the mean value and the standard deviation of the QT interval measurements for those leads. The measurements that remain out of the window $mean \pm 2.1 * STD$ and whose amplitudes are less than 0.1363 mv. are excluded from the measurements. It is assumed that, QT interval measurements can not change very much between leads although there is QT dispersion. $Mean \pm 2.1 * STD$ has been found to be the critical limit for elimination. If it is selected too high, the wrong measurements are not excluded. Otherwise, correct measurements are excluded.

The beats' parameters, which pass all of the checks, are written to the output file as the last measurement. -1 is written to the output file for un-measured leads. Figures 3.15 shows all the tests done in block diagram format.

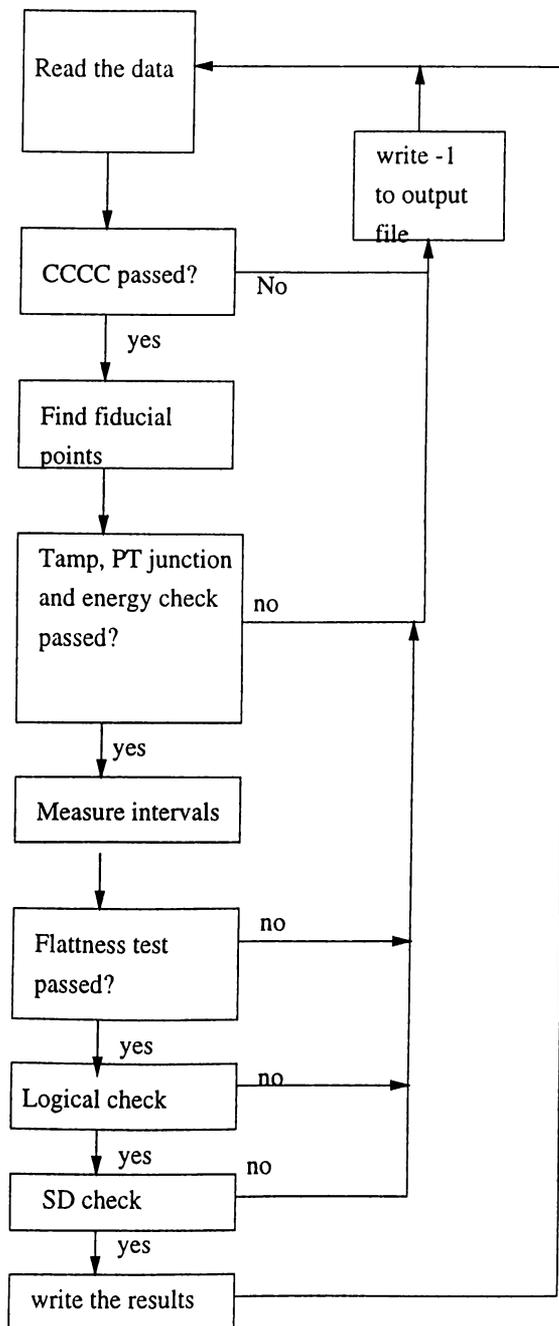


Figure 3.15: The T wave test Block Diagram

Chapter 4

Statistical Evaluation

4.1 Statistical Elimination

Although various checks and elimination were done for QT interval measurements, we can still have erroneous measurements due to strange T waves. These measurements can be corrected or eliminated using statistical methods. We process all of the leads separately using the same algorithm, which will be explained below.

A MATLAB program does this statistical process and gives the QTD trend as the output. We read the QT interval values for all leads to a matrix (12 by n : number of average beats) and heart rate tachogram from the file.

The peak exercise point is found as the point where heart rate is at maximum rate. The dynamic behavior and QT interval properties of the heart are different before and after the peak exercise, thus we will analyze these parts separately. As a physical fact, QT interval can not change abruptly and it is continuous at the peak exercise.

The statistical process is done for each lead individually. The number of QT interval measurements at the recovery phase is more than previous steps since

the noise and PT fusion are low at the recovery. The QT interval trend during exercise can be modelled by two different second-degree parabolas before and after peak exercise as seen in figure 4.1. These parabolas have no physical meaning but they can be used for statistical outlier rejection.

A second-degree parabola is fit to the recovery part of QT interval values for each lead. As the second step, we fit a second-degree parabola to exercise phase QT interval measurements satisfying the continuity fact at the peak exercise point. The parabolas are fitted if there are more than 8 measured QT intervals in each phase. If there are less than 8 measurements all of the measurements are eliminated since the number of measurements are not enough for QT interval parabola fitting. We exclude the measurements which align outside the $\pm 8\%$ of these parabolas. The parabolas model the QT interval values during exercise as seen in the figures 4.1 and 4.2. The measurements, which are not close to these parabolas, are excluded. The figures also show the $\pm 8\%$ above and below the parabola.

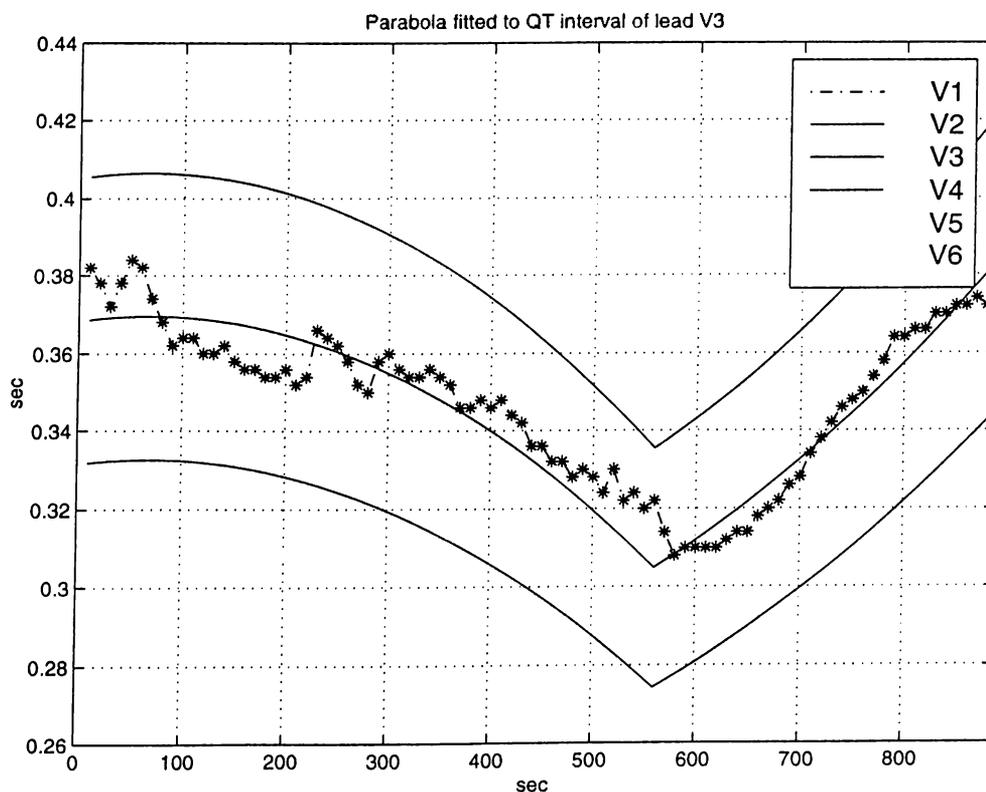


Figure 4.1: QT intervals and parabola fit to V3

After the elimination of QT some intervals, we estimate the QT intervals

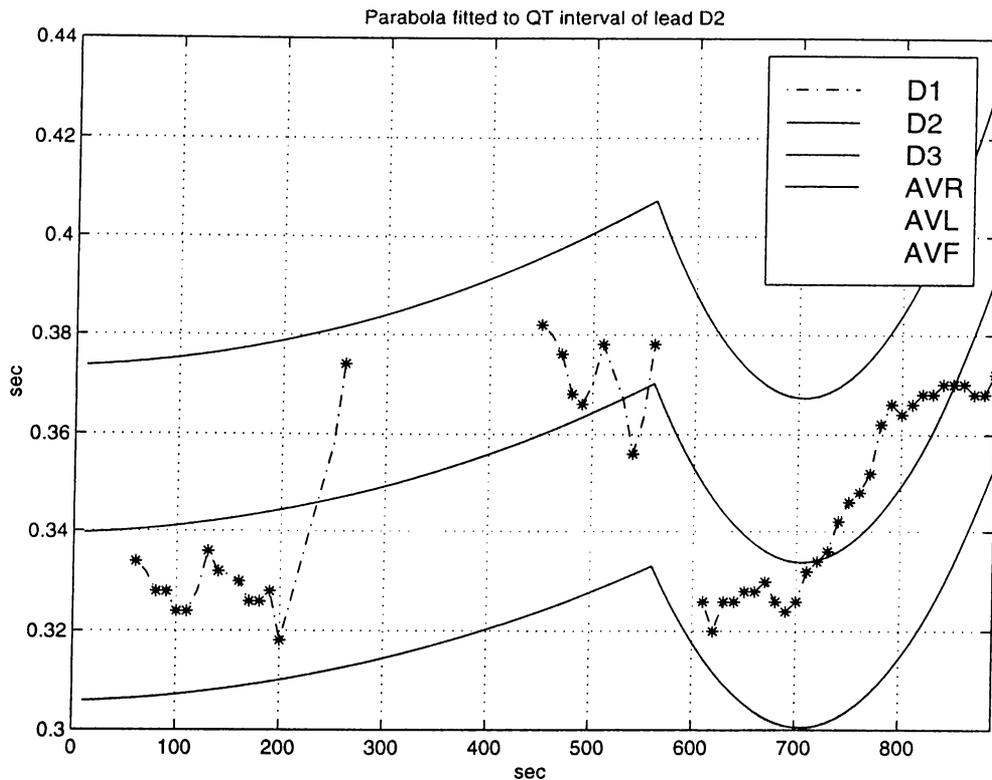


Figure 4.2: QT intervals and parabola fit to D2

that are not measured using the whole QT interval trend. We combine two measurements of a lead with a line if there are less than 8 unmeasured QT intervals between these two measurements. If not, we do not estimate these intervals. This line estimates the QT intervals, which are excluded or not measured. This process is a result of continuity fact. If the two points are in different phases of the exercise test, we do not estimate the data points between them using a line since the dynamics of QT interval in these phases are different. The measurements that can not be estimated remains unmeasured. They are defined as 'Not A Number' in MATLAB and are not plotted in the figures.

In Figure 4.2 the stars show the measurements done and the line between stars shows the estimated measurements. We did not estimate the measurements between seconds 300 and 400 since the number of unmeasured points between them exceeds eight. In this figure, the number of measurements for recovery phase is more than the number of measurements in exercise phase since the noise level is low in recovery phase. Thus, we first fit a second-degree parabola to that phase. At $t=200$ sec. the exercise progresses one step, the

heart rate increases, ischemia occurs so an incline in QT interval at D2 is seen.

In figure 4.1 the lead V3 is very clean so we had all the measurements done. In this figure, we can observe the continuity fact.

As a result of these processes, we have QT interval trends for 12 leads or less.

4.2 Finding the Lead Pairs Giving the Maximum QTD

In classical QTD approaches [13], QTD is measured between leads giving the maximum QT interval difference at that time. That maximum difference is called QTD. At different time instants, different lead pairs could give maximum QT difference. QTD is calculated at two points at rest and at peak exercise. Mathematically;

$$QTD(n) = \max(QT_{measured}(n)) - \min(QT_{measured}(n)) \quad (4.1)$$

n is the time instant. This approach gives very noisy QTD trends and not suitable for statistical process since at different time instants, different lead pairs are used for QTD calculation. For ex. at $t=1$ D1,V6 ; at $t=2$ D2,V6 ; at $t=3$ V4,V6 lead pairs can lead the maximum QT difference.

Figure 4.3 shows the QTD trend obtained by classical approach, our approach, and the heart rate for a healthy man. The phase where the heart rate decreases is the recovery phase. The QTD should not be high since that trend belongs to a healthy man. However, if we look at the classical approach's QTD trend, there is a high QTD (up to 60 msec.) during recovery phase. On the other hand, the QTD trend obtained by our approach gives low QTD during recovery as expected.

In this study, a different approach is proposed for QTD trend measurement and evaluation. This is the first study where QTD is measured throughout

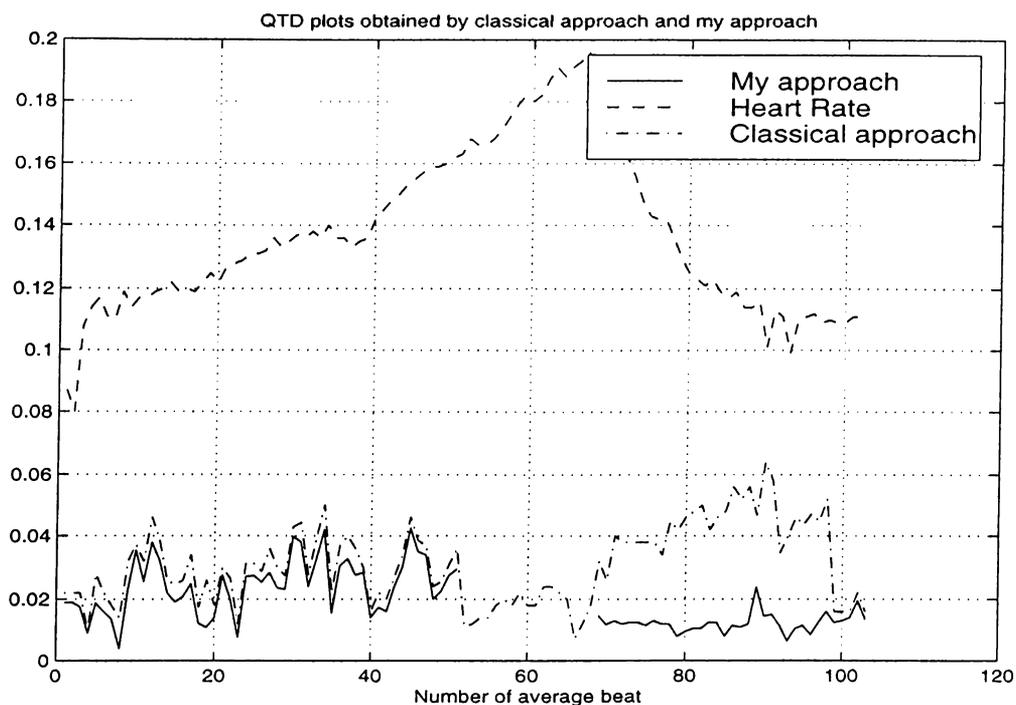


Figure 4.3: QTD trends obtained by classical and our approach

the exercise test and is evaluated for same lead pairs. We first find the difference of QT intervals for all possible lead pairs (D1,D2; D1,D3 ; D1,V6; D2,D3;.....;D2,V6 ;...; V4,V5 ; V4,V6 ; V5,V6). 66 QT difference vectors are obtained. If there is no measurement for a QT interval, the difference not calculated.

The exercise phase of each QT difference vectors are divided into 3 equal pieces in time. The mean of the third piece for all 66 vectors is calculated. If there exists a high QTD between leads in that patient, this third piece should yield the maximum mean QT difference because it is just before the peak exercise. Ischemia is maximum at peak exercise.

We obtain 66 mean values as a result of this process. Each of these mean values belongs to a specific lead pair. We sort these values in descending order and get the first 5 mean values from the list each belonging to a lead pair. These lead pairs give the maximum QTD trend. We have found the first five maximum QT difference vectors each belonging to a specific lead pair unlike the previous approaches. We calculate the mean of these five vectors (they are

equal length in time) and refer it as QTD trend. We investigate if this QTD trend can be used as an additional diagnostic tool to ST segment analysis in exercise ECG diagnose process.

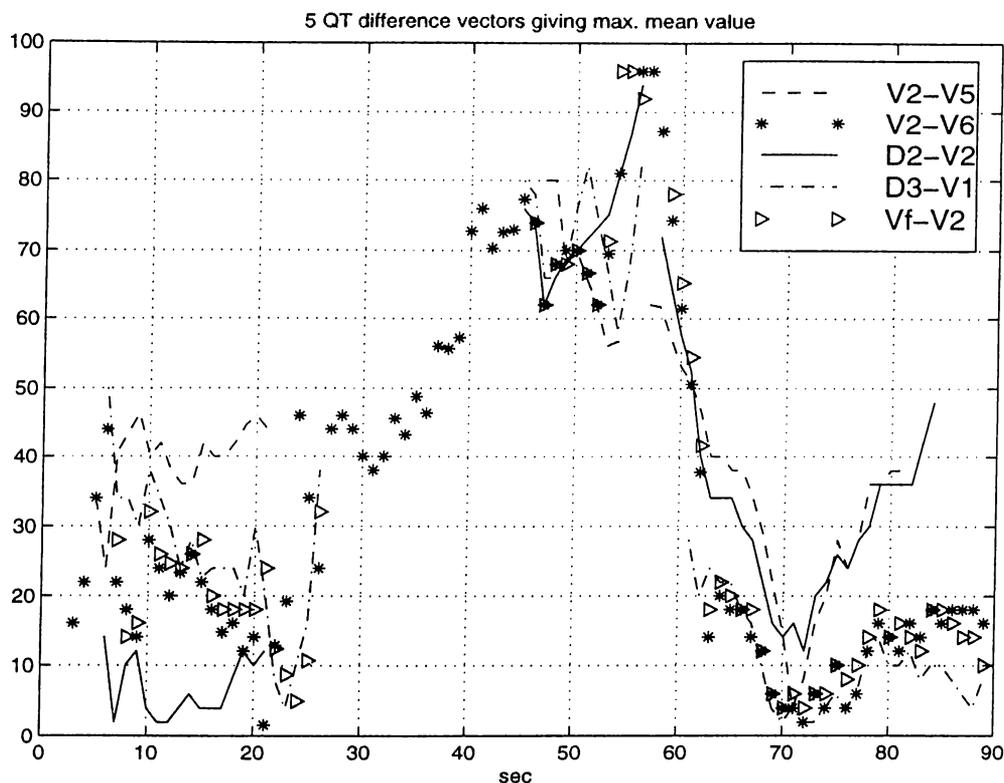


Figure 4.4: QTD vectors for five maximum mean values

Figure 4.4 shows the five maximum QTD trend vectors. Each vector belongs to a lead pair as seen in the figure. The measurements between seconds 40 and 60 are in the third piece and gives the highest QTD mean value when compared to pieces 1 (between 0-20) and 2 (between 20-40).

4.2.1 Steps to Obtain QT Dispersion Trend

1. Read QT intervals from the files with extension .PAR
2. Detect the peak exercise point (The instant where heart rate reaches to maximum)
3. Fit parabola to exercise and recovery phase measurements, if more than 8 QT intervals are measured in each individual phase.

4. Exclude the measurements which remain outside the region $\pm 8\%$ of fitted parabola.
5. Estimate the unmeasured QT intervals if the number of unmeasured QT intervals between them is less than 8, else leave them empty (NaN).
6. Obtain 66 QT difference vectors for all possible lead pairs.
7. Divide the exercise part of the QT difference vectors into 3 slices and find the mean value of the third slice for each 66 vectors.
8. Sort these mean values in descending order (Each for a lead pair).
9. Take the first five lead pair from the list.
10. Calculate the mean value of these five QT difference vectors to obtain the QTD trend.

Chapter 5

Results and Conclusions

QTD trends of 89 records have been obtained in this study. These patients are distributed into six groups according to their properties. Some of the patients had coronary angiography results, which is an invasive diagnostic tool for ischemic heart disease. If a patient has a POSITIVE angiography result, it means that he has ischemic heart disease.

The most important subject is defining the criteria while diagnosing a patient QT POSITIVE. The level of QTD or an increase in QTD level can be used as a criterion. If the level of QTD will be used for diagnosis, a threshold must be defined. We have defined this threshold as 50 msec. In this study, a patient is called QT POSITIVE if the QTD trend increases above 50 ms. as the exercise progresses or there is a constant QTD trend above threshold.

The cardiologists examine all the ST plots in time as a diagnostic tool and QTD trend plot can also be used like that. This is a different approach since in previous works, researchers have found the QTD at rest and at exercise and used these two numbers for diagnosis. In this study, we have QTD trend for all instants of exercise ECG test.

The patients whose QTD trend remain under a threshold or have constant low-level QTD are classified as QT NEGATIVE. The patients having increasing

QTD trend but below a threshold must be investigated more. Since we did not have angiography data for those patients, we could not investigate them further. Four of the patients have been performed coronary angiography for the final diagnosis. This is a very small number to make a statistical analysis based on specificity and sensitivity of the exercise ECG test when classified using QTD trend.

1. STN, QTN, A-; Negative ST diagnosis, Negative QTD diagnosis, No available angiography data

These patients are classified as healthy subjects. Figure 5.1 shows the QTD trend of one of these subjects.

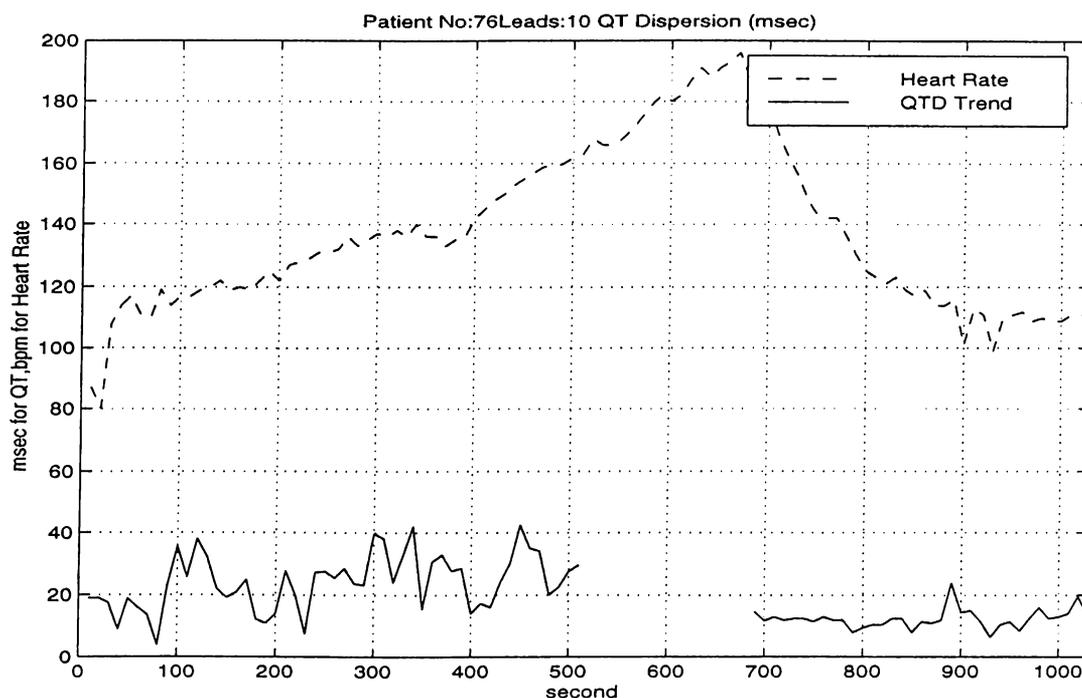


Figure 5.1: QTD and Heart Rate ST=- QT=- A=?

Although the number of ischemic patients is low in this study, we have QTD trend of 65 normal subjects. We can examine how a healthy subject's QTD trend looks like. Their QTD trend remains under 50 ms. in each step of exercise or it increases a little amount at step change instants.

2. STP, QTP, A+; Positive ST diagnosis, Positive QTD diagnosis, Positive angiography

These patients have ischemia verified by coronary angiography. Patients 30 and 3044 are in this group. We can see the QTD trend of these patients in figures 5.2 and 5.3.

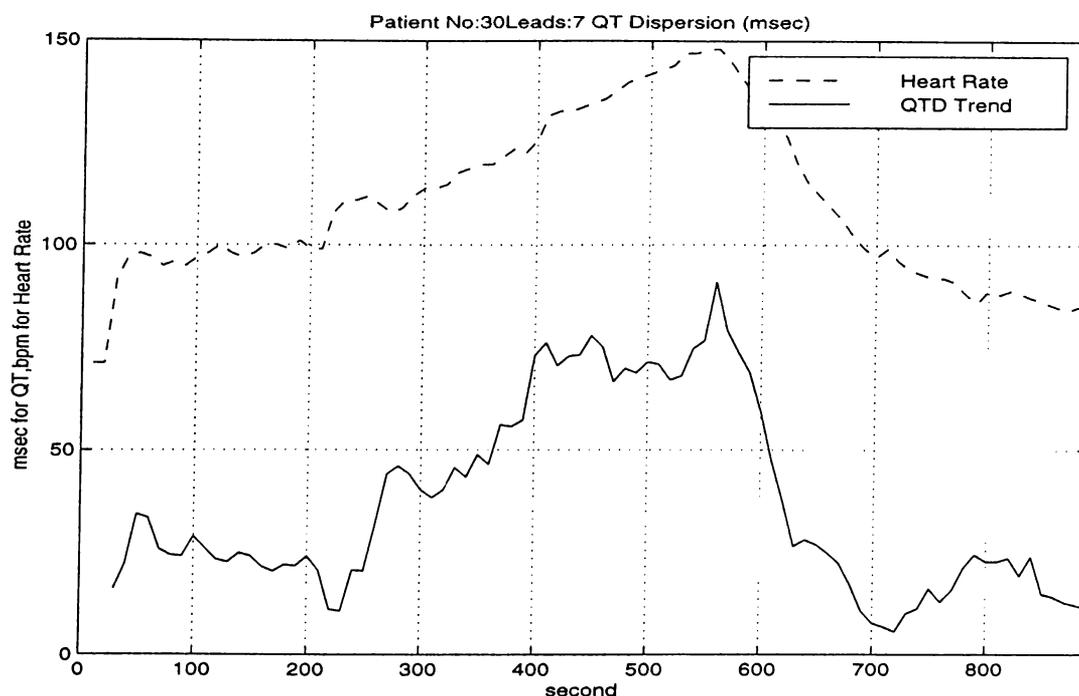


Figure 5.2: QTD and Heart Rate ST=+ QT=+ A=+

As seen the QTD trends of these patients are different from the healthy subject's QTD trend. In order to verify this discrepancy statistically, the number of patients in this group is not enough.

In figure 5.2 the step change of the exercise protocol can be seen in heart rate trend. At $t=200,380$ sec. the exercise step progress and heart rate increases to pump more blood to body. At $t=560$ sec. the exercise test ends and heart rate decreases. The patient whose QTD trend is shown in figure 5.2 has a high level of ischemia, which was verified by coronary angiography. The QTD trend of this patient increases like heart rate as the exercise progress and decreases when test ends. We know that, as the exercise test progresses the ischemia level of the heart increases. Because of the increased ischemia, QTD increases. The QTD trend of this patient verifies this physical fact.

3. STP, QTP, A?; Positive ST diagnosis, Positive QTD diagnosis,

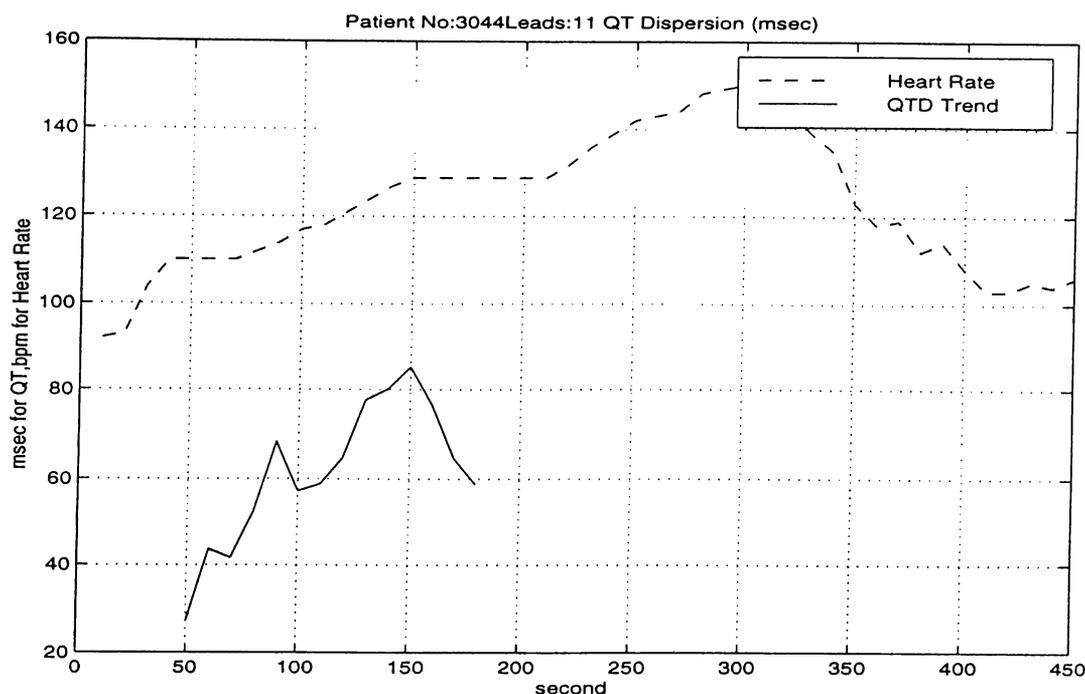


Figure 5.3: QTD and Heart Rate ST=+ QT=+ A=+

No angiography

These patients have positive QTD and ST analysis results, which show that they have a high level of ischemia. They have no coronary angiography result to verify this. However, we can classify them in group 2. Figure 5.4 shows the QTD trend of one of these patients. The QTD trend is like the QTD trend in figure 5.2. There is no measurement between 300 and 500 sec.

4. STP, EXT; Positive ST diagnosis, Have External effects

Patients having positive ST diagnosis and having drug therapy or had taken surgical therapy before the test (PTCA, stent). Drugs (Beta-Blockers, Ca Blockers), PTCA and stent reperfuse the veins and decrease the level of ischemia in the heart. Verifying this fact, most of the patients in this group have low QTD trend but we do not evaluate the QTD trend of patients having external effects. Patients in this group have been diagnosed as ischemic already. We want to investigate if the QTD trend can be used as a diagnostic tool at the first stage.

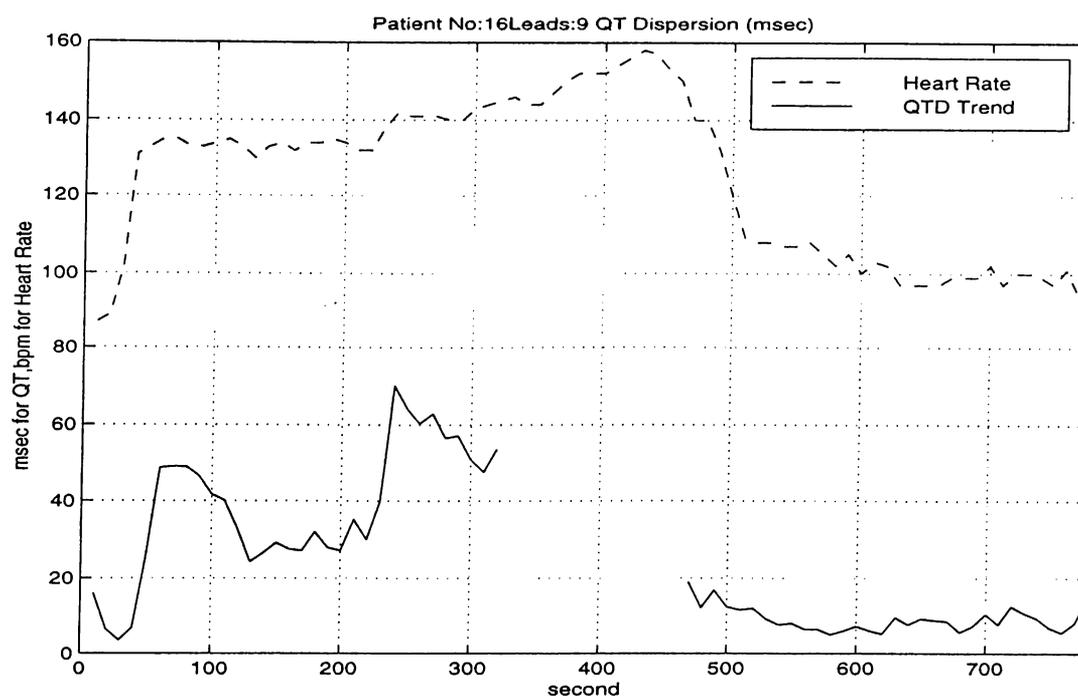


Figure 5.4: QTD and Heart Rate ST=+ QT=+ A=?

The affectivity of medical or surgical therapy to reperfuse the veins can be investigated by looking at the exercise QTD trend.

Figure 5.5 shows the QTD trend of a patient who has taken beta-blocker before the test. Although this patient has a high level of ischemia verified by coronary angiography, the QTD trend is normal. The drugs that the patient has taken before exercise test can effect the QTD trend. Thus, the patients in that group must be examined further.

5. STN, QTP, A?; Negative ST diagnosis, Positive QTD diagnosis, No angiography

The patients in that group have negative ST diagnosis, positive QT diagnosis. None of the patients has angiography result since ST negative classified patients do not take angiography. These patients should be investigated more carefully to see if they have any other heart disease different from ischemia. For example, the QTD trend of patients who have arrhythmia risk increases. They must have electrophysiologic test to examine the conduction abnormalities of the heart and find the arrhythmia risk. Figure 5.6 shows the QTD trend of a

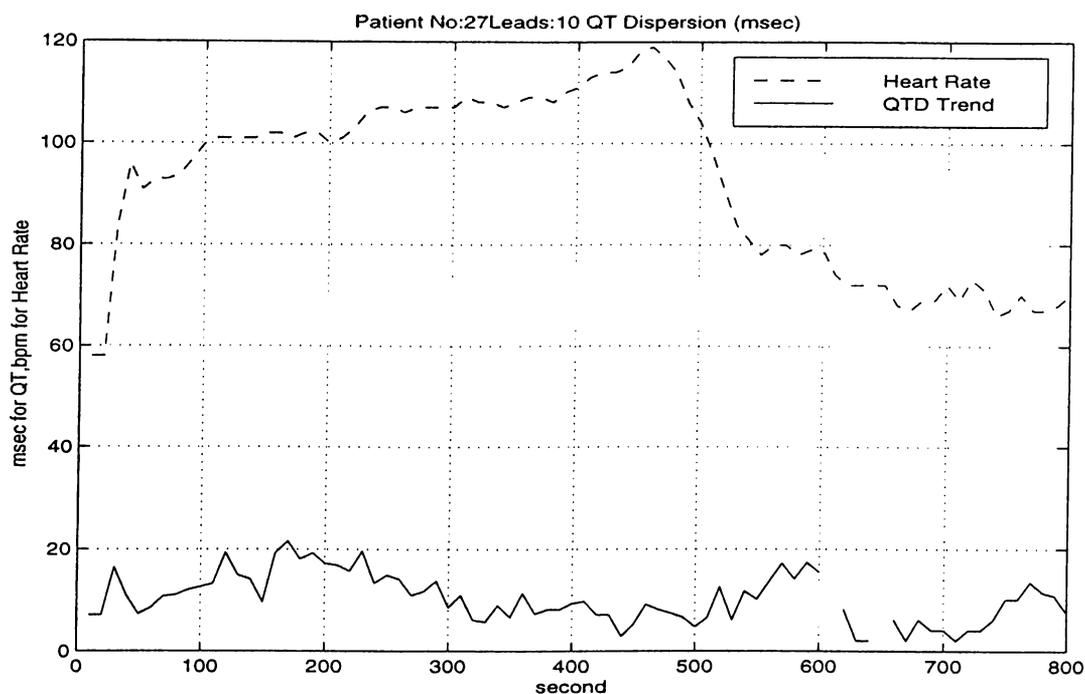


Figure 5.5: QTD and Heart Rate ST=+ QT=+ EXT A=+

patient in that group.

6. STP, QTN, A? ; Negative ST diagnosis, Positive QTD diagnosis, No angiography result

These patients have been classified as having ischemia by cardiologists with ST segment analysis. One of the patients in this group had taken coronary angiography. If we examine the QTD trend of these patients, we diagnose them as non-ischemic.

Patient 3068 has been diagnosed as ischemic by ST segment analysis. However, she is not ischemic according to QTD trend analysis and that has been verified by coronary angiography. This was a false positive diagnosis of exercise ECG test using ST segment analysis. If we had used the QTD trend as an additional diagnostic tool to ST segment, this patient would not have coronary angiography, which is a high-risk invasive diagnostic tool. As the false-positive rate of exercise ECG test decreases and the specificity increases.

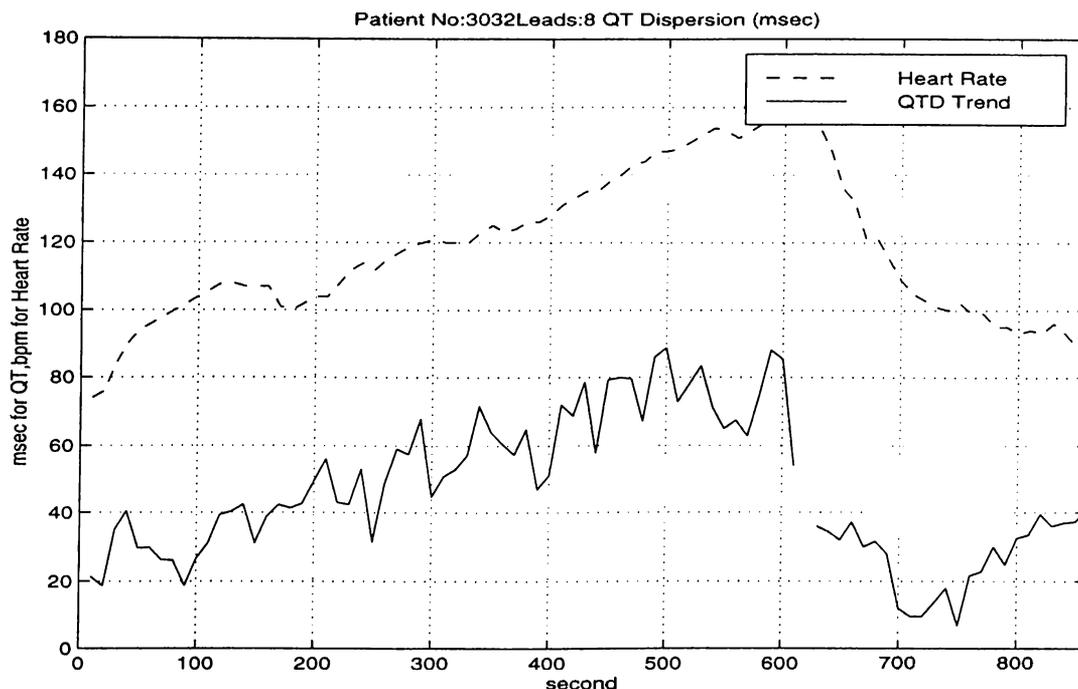


Figure 5.6: QTD and Heart Rate ST=- QT=+ A=?

This was shown previously for women with a classical approach QTD analysis [7]. They have calculated the QT intervals only at rest and peak exercise measuring the QT intervals manually. Measuring the QTD at only one point during peak exercise is not a good approach since the noise and PT junction artifacts occur more at the peak exercise point.

The false-positive rate of exercise ECG test for women, when diagnosed with ST analysis, is high due to different hormones in the women' blood. Most of the patients in group 6 are (4 of 6) women which verifies this physical fact.

If we want to decrease the false positive rate of the exercise ECG test, we should diagnose a subject's test as POSITIVE if his QTD trend and ST analysis are positive at the same time. If the purpose is not to miss the ischemic patients, we should diagnose the test as positive if QTD trend or ST analysis results are positive. Sometimes the ST analysis can miss the ischemic patients and classify them as negative, which is a very dangerous situation.

The sensitivity of exercise ECG test is %55 and specificity is %64.

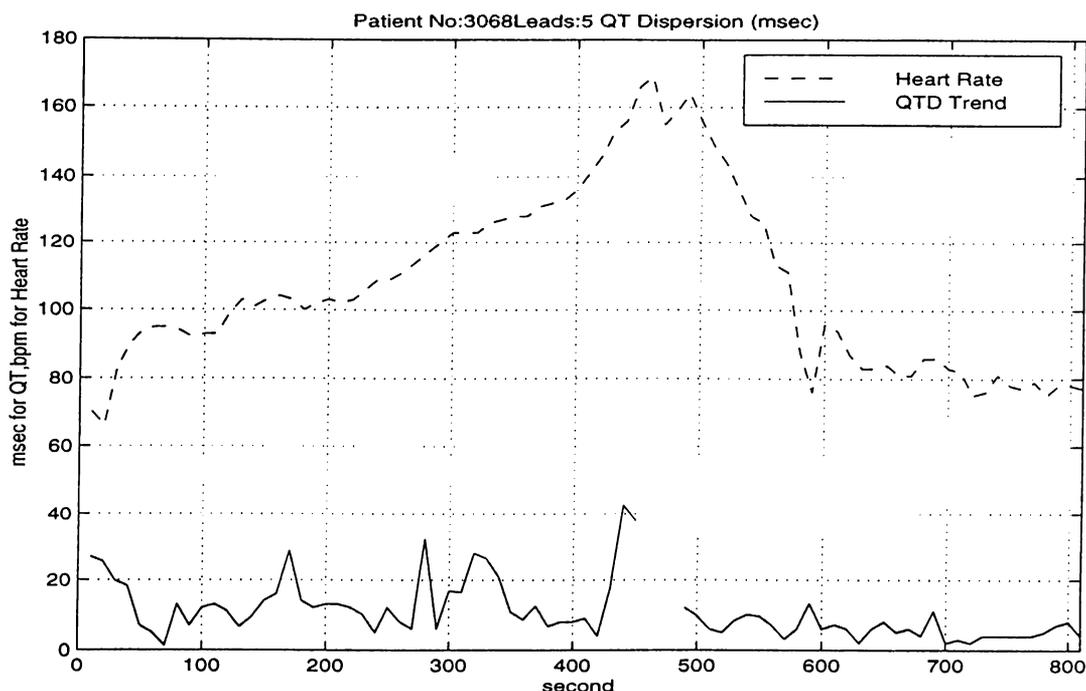


Figure 5.7: QTD and Heart Rate ST=+ QT=- A=-

$$Sensitivity = \frac{True\ Positives}{True\ positives + False\ negatives} \quad (5.1)$$

$$Specificity = \frac{True\ Negatives}{False\ Positives + True\ positives} \quad (5.2)$$

If we union the QTD analysis and ST segment analysis sets the sensitivity of the test increases. On the other hand, if we take the intersection set of ST analysis and QTD trend results sets, specificity increases and sensitivity decreases [7]. Thus, there is a trade off between these two approaches. The decision is based on the purpose of the cardiologist.

The results of this study indicate that, QTD is increased during exercise induced myocardial ischemia in patients with significant coronary artery disease. The figures in Appendix A provide support for the hypothesis that QTD may reflect the regional differences in ventricular recovery time or repolarization, which is very sensitive to ischemia.

This study indicates that the measurement of QTD in patients of possible

ischemia is a useful adjunct in the interpretation of exercise ECG and may markedly improve the diagnostic accuracy of exercise ECG test.

5.1 Future Work

The number of patients to make a statistical conclusion about the results is not enough. Especially the number of coronary angiography results should be increased to see if the patients have ischemia or not using QTD analysis. As a future study, more records from the patients should be taken who has angiography results.

The measurement errors are caused by the misdetection of the T peak. We should use different parameters while measuring the QT intervals of different subjects. In order to do this we should classify the T wave morphologies, if it is elevated, depressed, biphasic or normal. If we measure each kind of T wave with more suitable parameters, the measurement errors decrease. As a future study a T wave classification algorithm should be proposed and the algorithm presented in this study should be run with different parameters for each kind of T wave.

As another study, the QT intervals can be measured from 2 or 3 orthogonal [17] components of SVD output. For that, we must investigate if the QTD information is carried by these orthogonal components or not. The effect of SVD on T wave must be investigated further as a future study.

Appendix A

QTD Trend Plots of Records

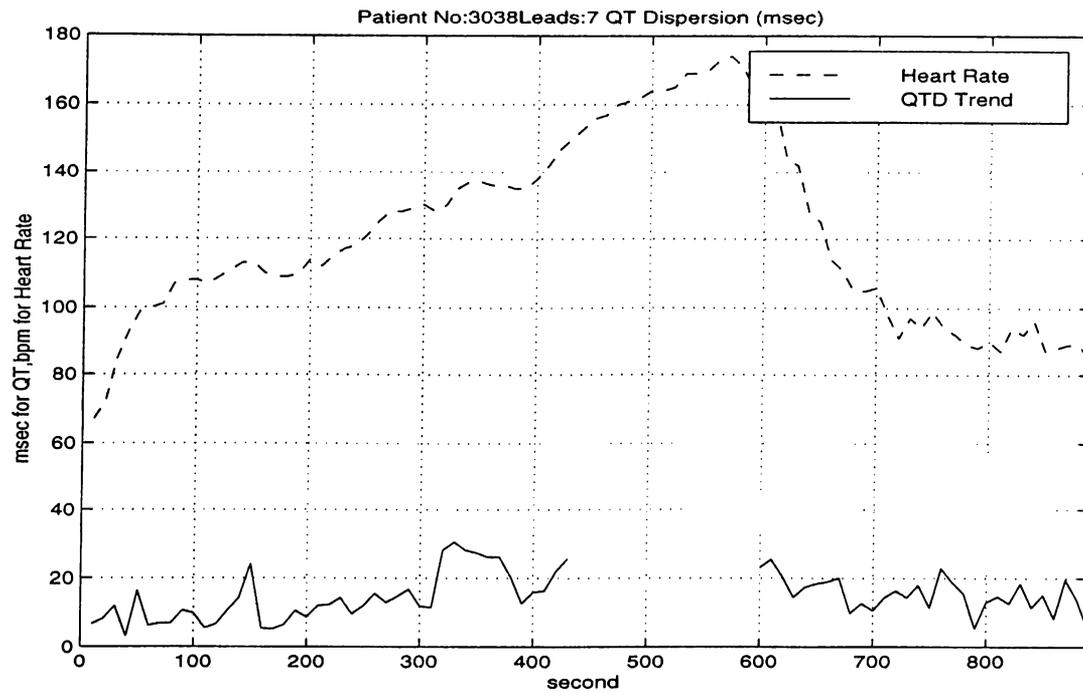


Figure A.1: QTD and Heart Rate for patient 3038 ST=- QT=- A=?

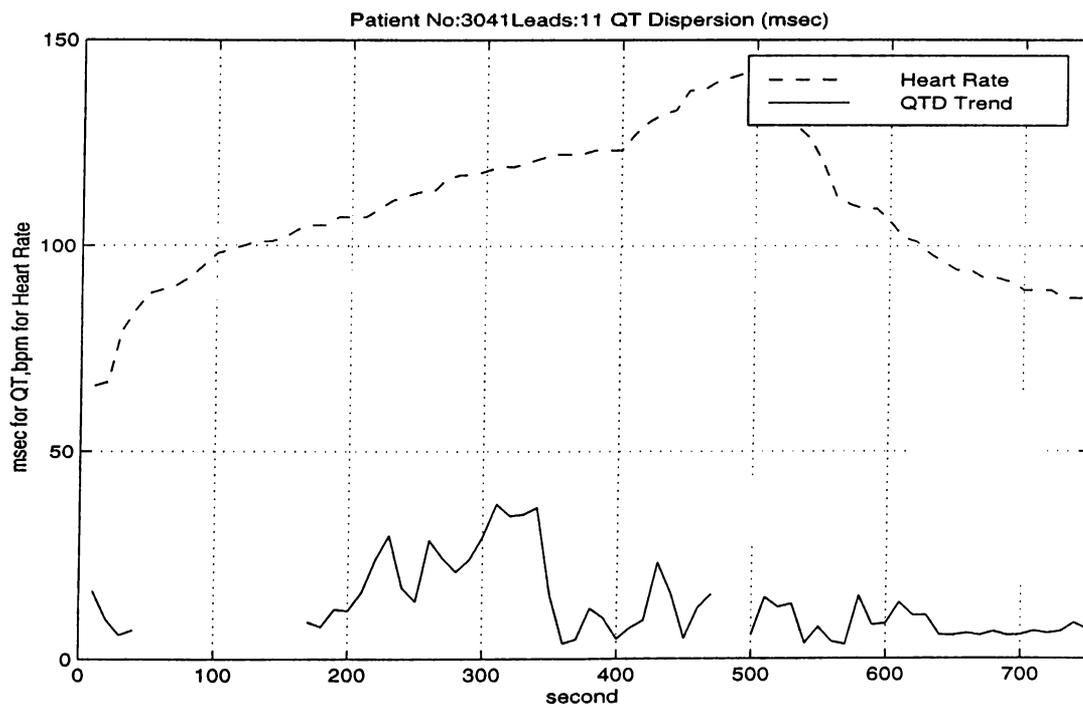


Figure A.2: QTD and Heart Rate for patient 3041 ST=- QT=- A=?

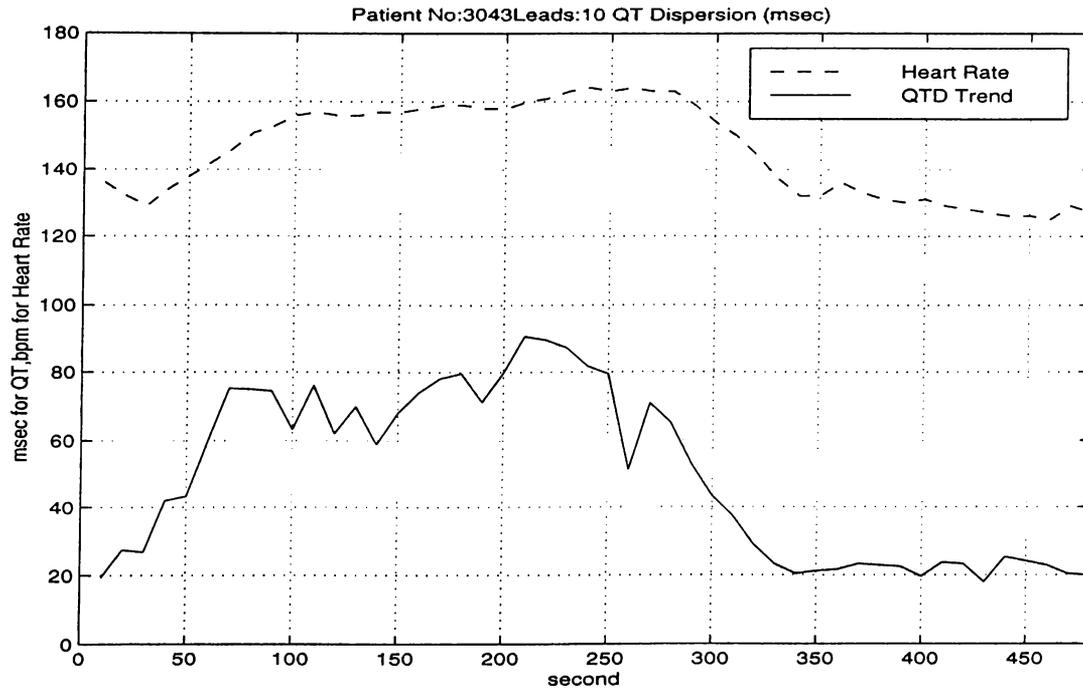


Figure A.3: QTD and Heart Rate for patient 3043 ST=- QT=- A=?

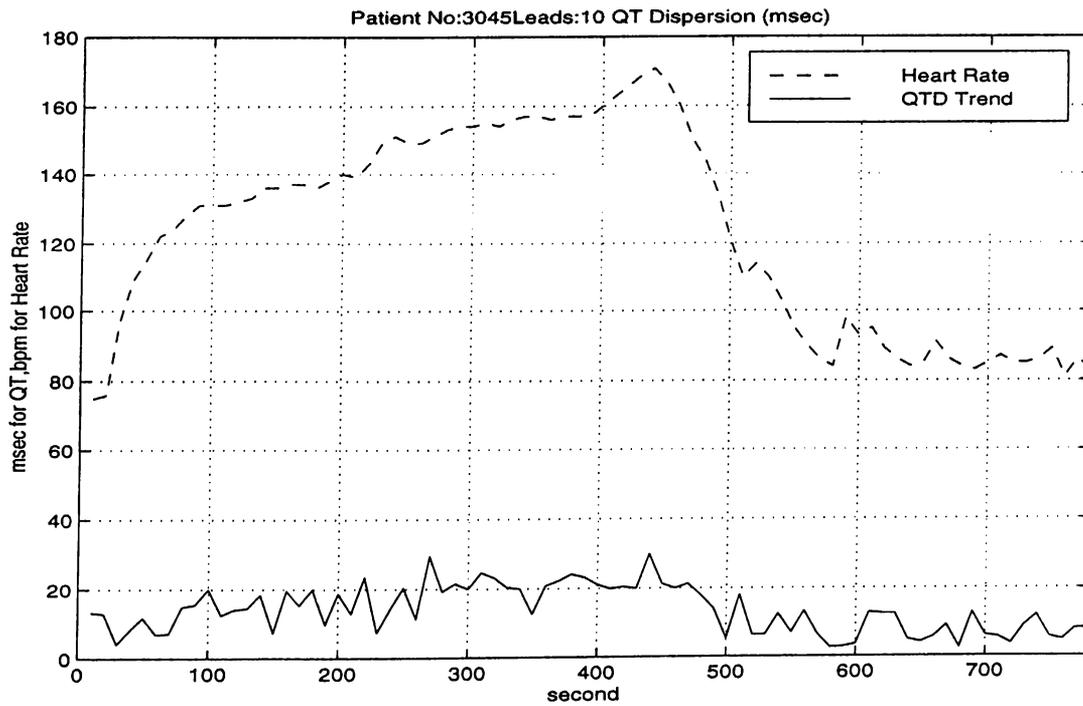


Figure A.4: QTD and Heart Rate for patient 3045 ST=+ QT=- A=?

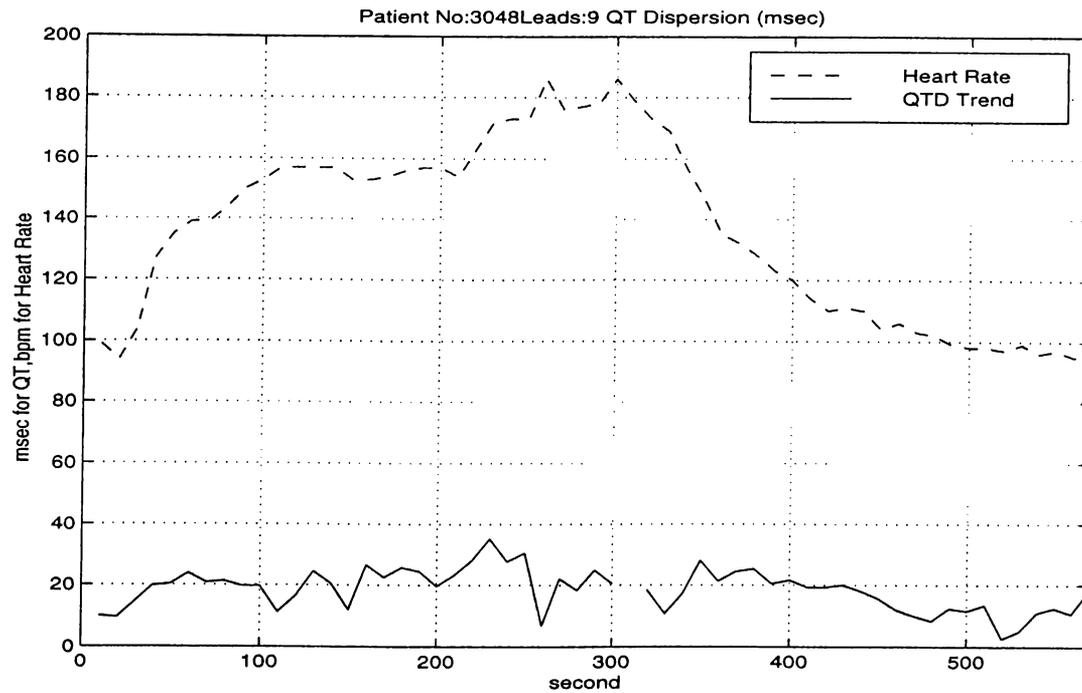


Figure A.5: QTD and Heart Rate for patient 3048 ST=- QT=- A=?

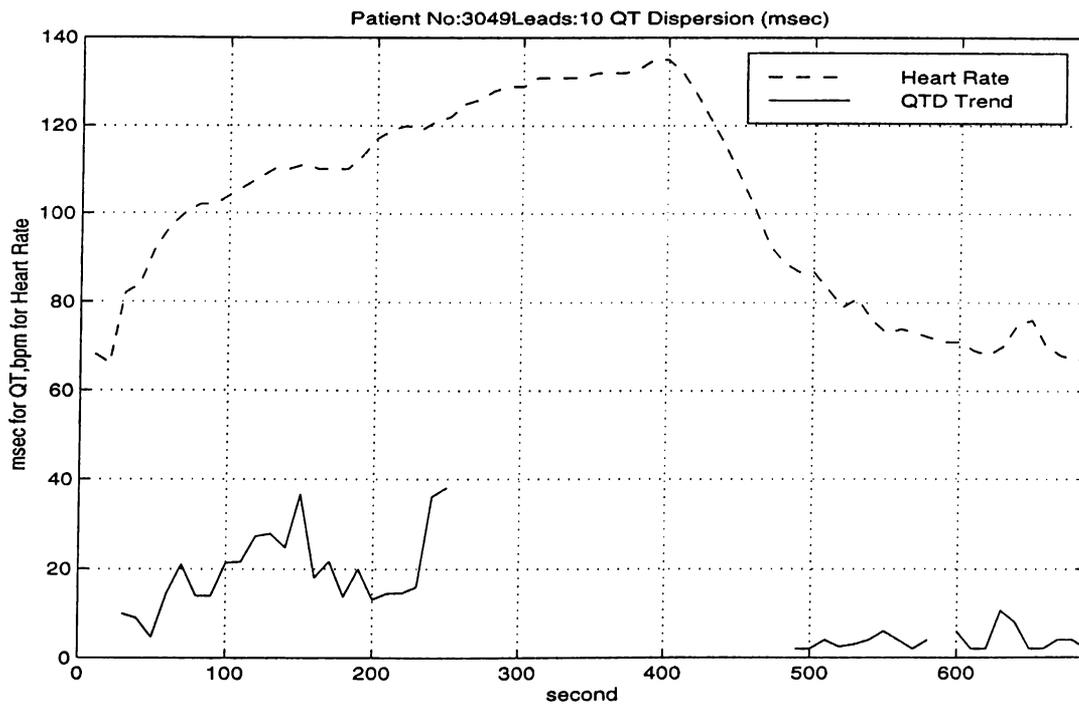


Figure A.6: QTD and Heart Rate for patient 3049 ST=- QT=- A=?

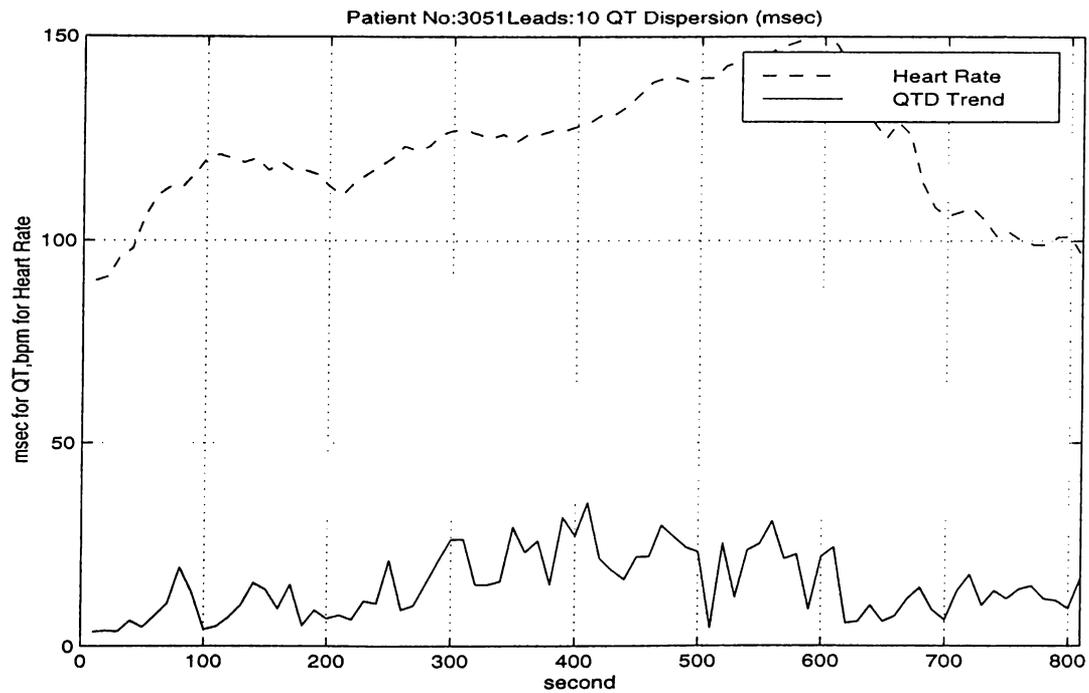


Figure A.7: QTD and Heart Rate for patient 3051 ST=- QT=- A=?

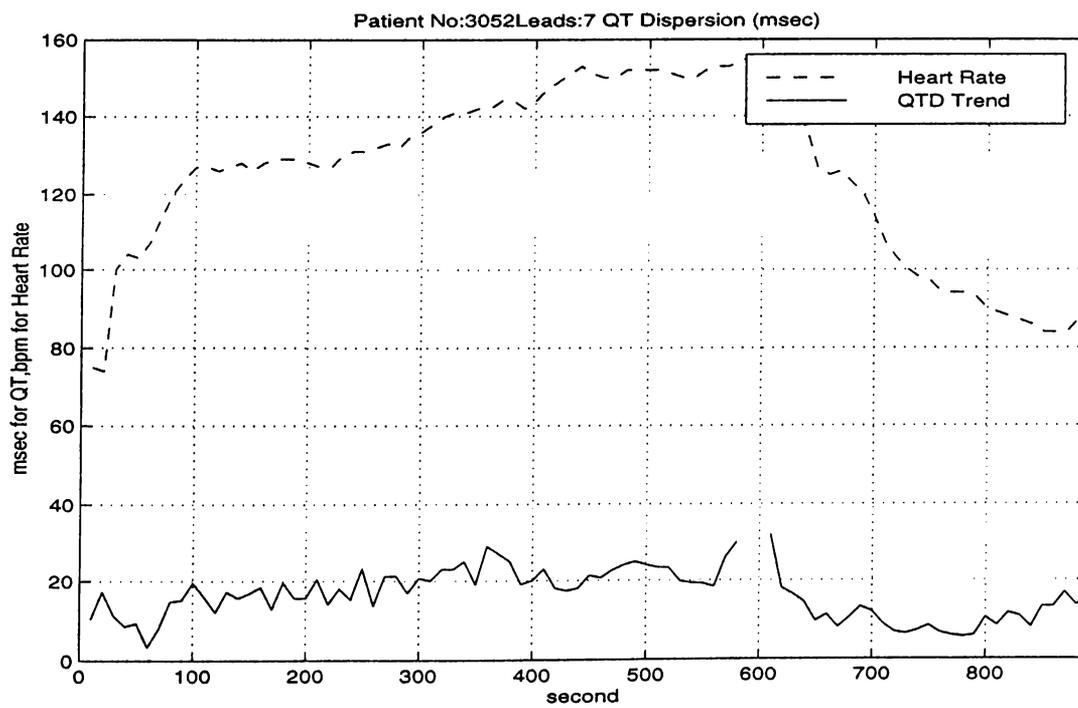


Figure A.8: QTD and Heart Rate for patient 3052 ST=- QT=- A=?

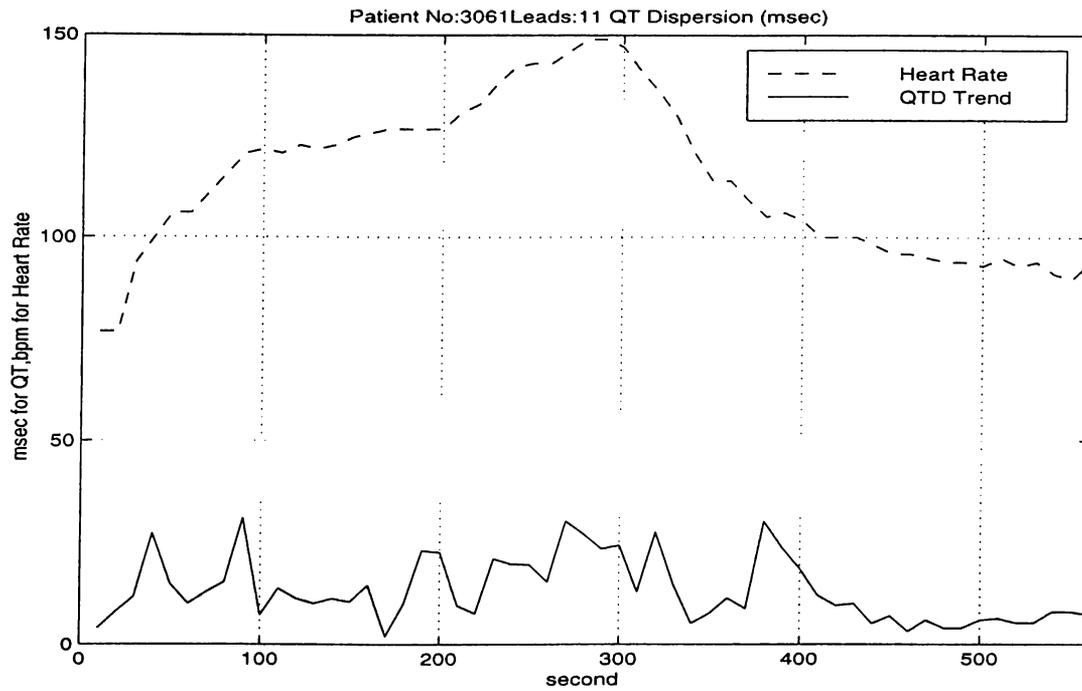


Figure A.9: QTD and Heart Rate for patient 3061 ST=- QT=- A=?

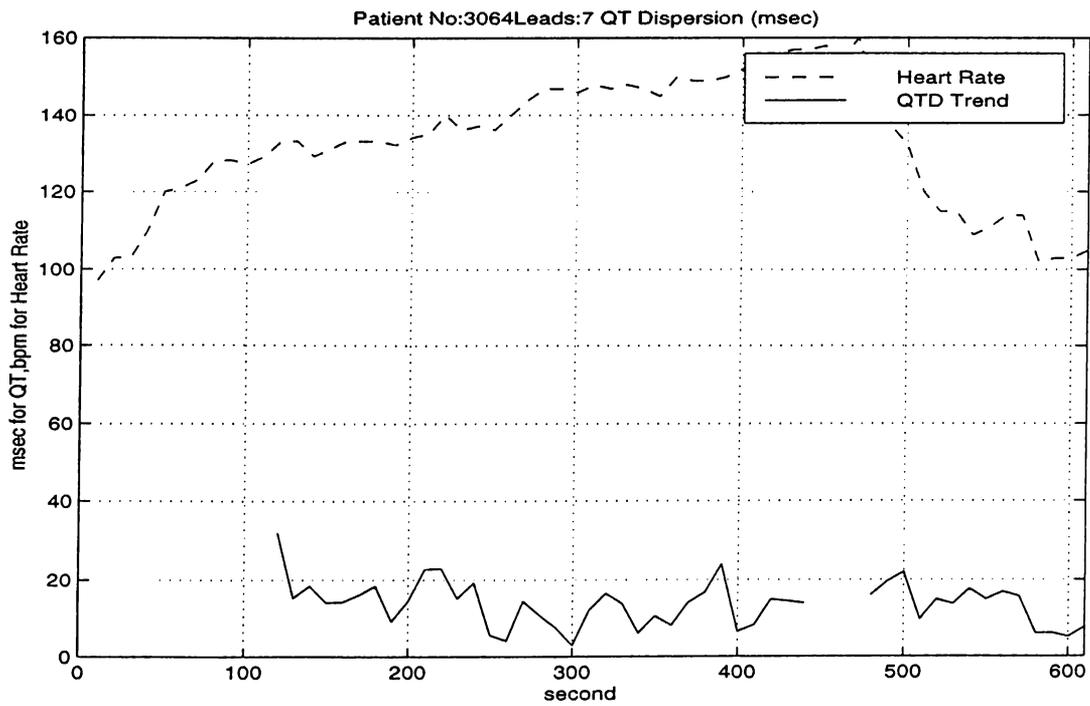


Figure A.10: QTD and Heart Rate for patient 3064 ST=- QT=- A=?

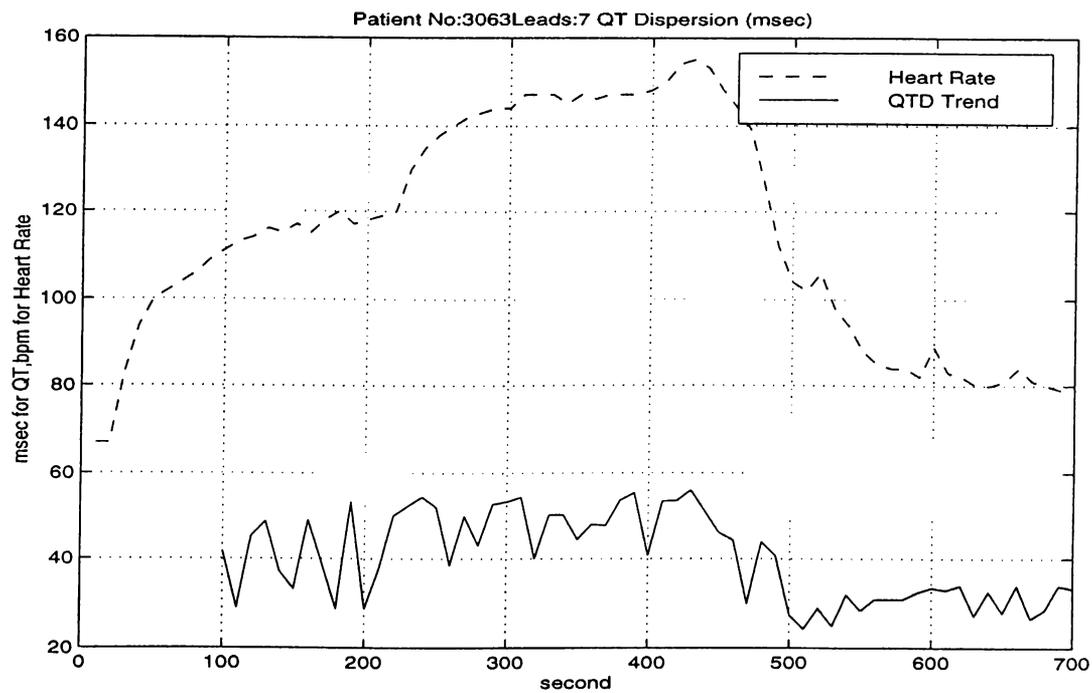


Figure A.11: QTD and Heart Rate for patient 3063 ST=- QT=- A=?

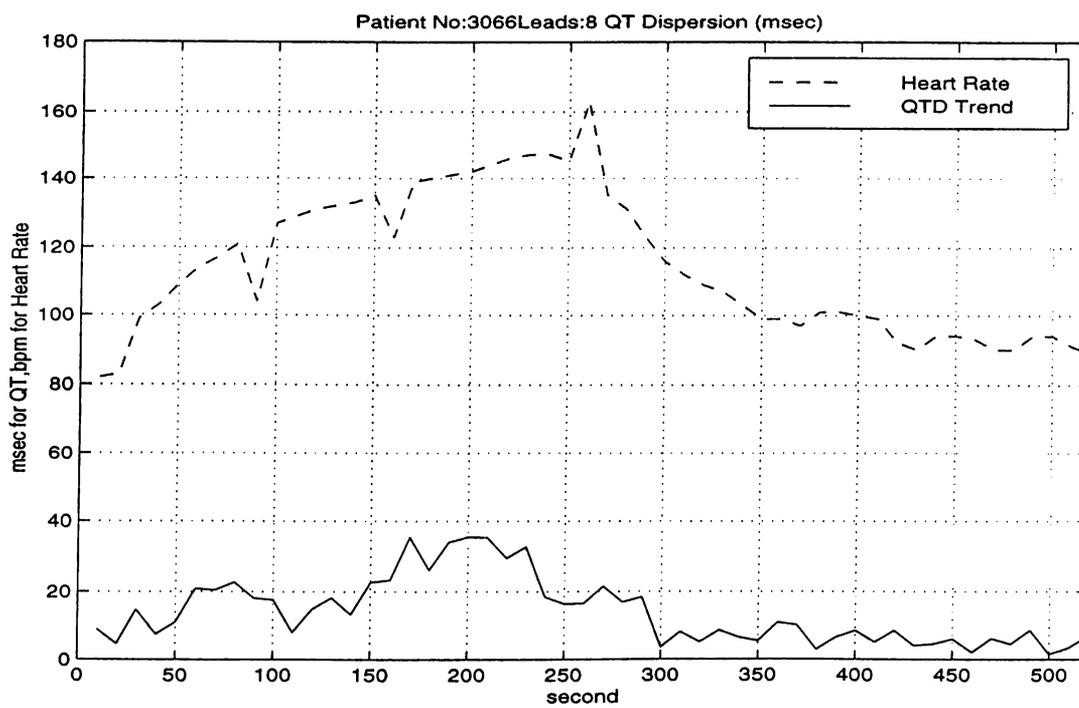


Figure A.12: QTD and Heart Rate for patient 3066 ST=- QT=- A=?

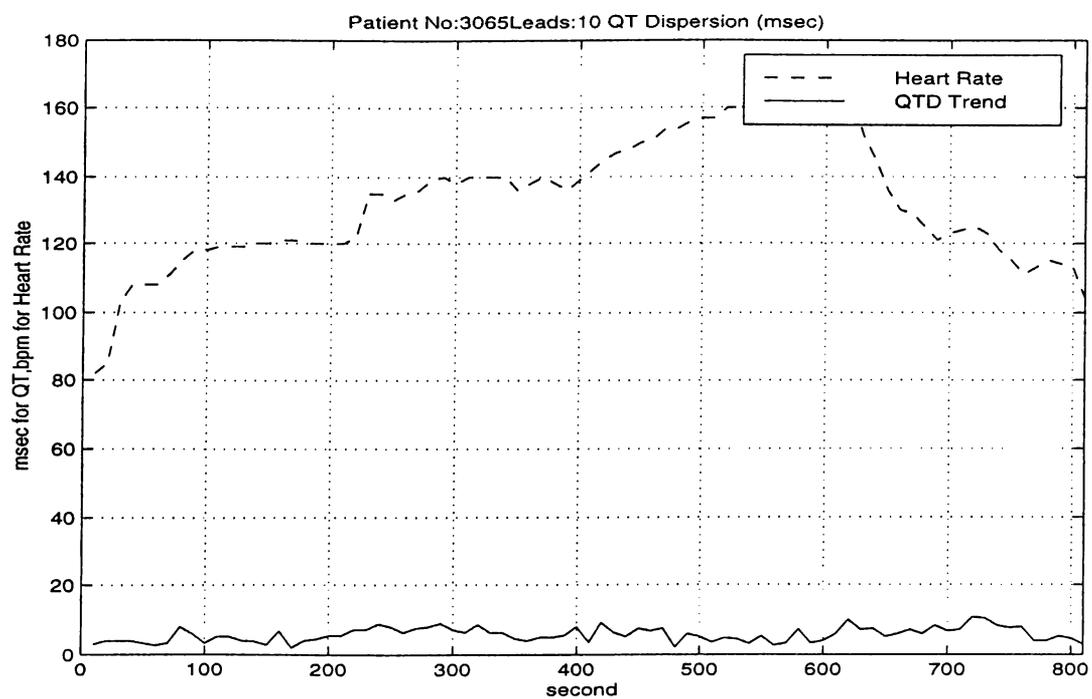


Figure A.13: QTD and Heart Rate for patient 3065 ST=- QT=- A=?

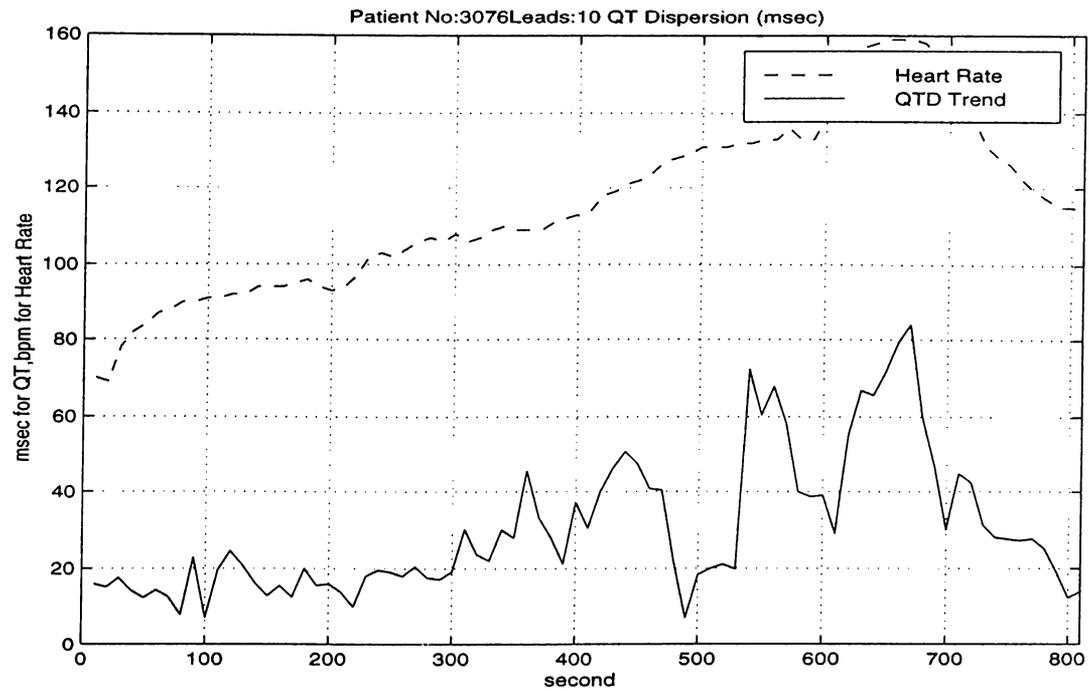


Figure A.14: QT Dispersion and Heart Rate for patient 3076 ST= QT= A=?

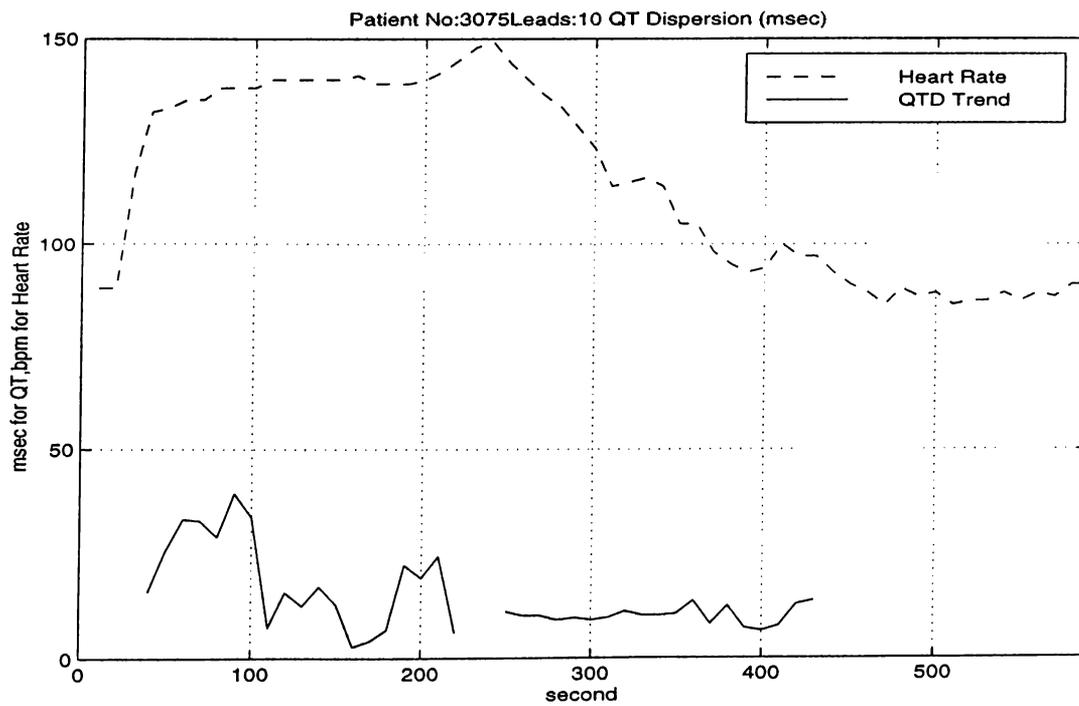


Figure A.15: QT Dispersion and Heart Rate for patient 3075 ST= QT= A=?

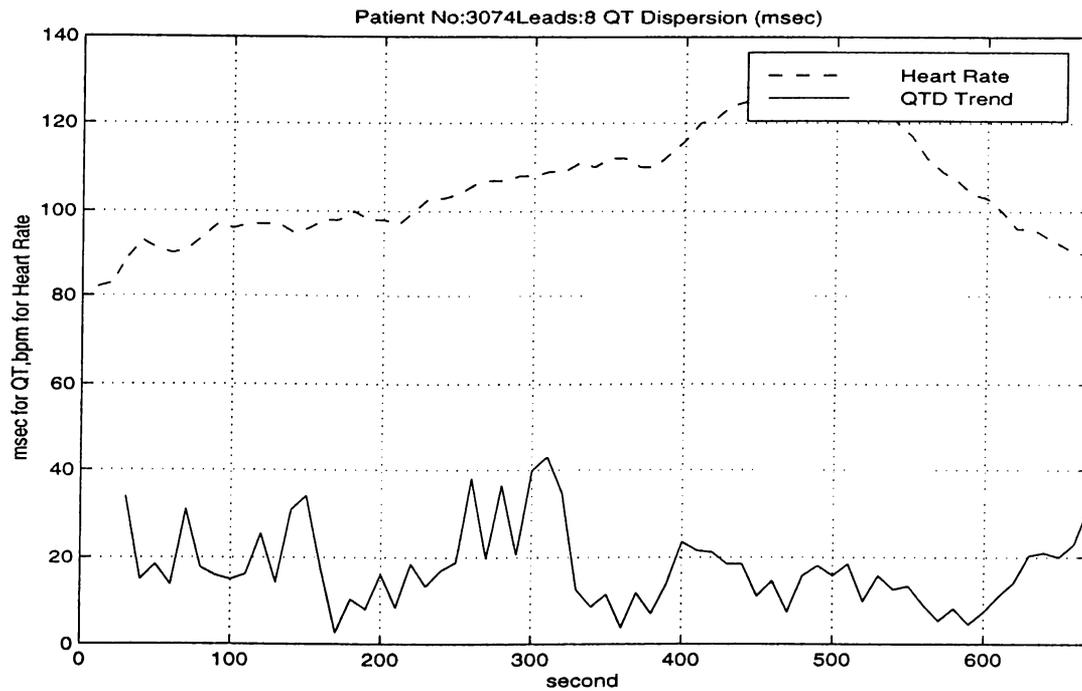


Figure A.16: QTD and Heart Rate for patient 3074 ST=- QT=- A=?

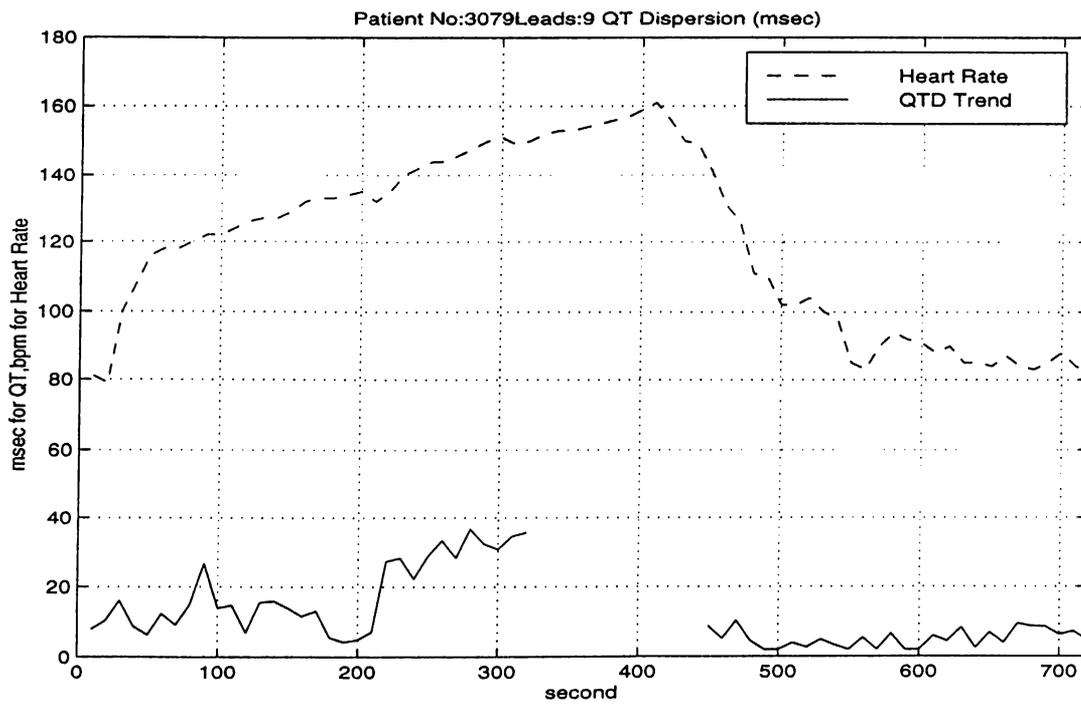


Figure A.17: QTD and Heart Rate for patient 3079 ST=- QT=- A=?

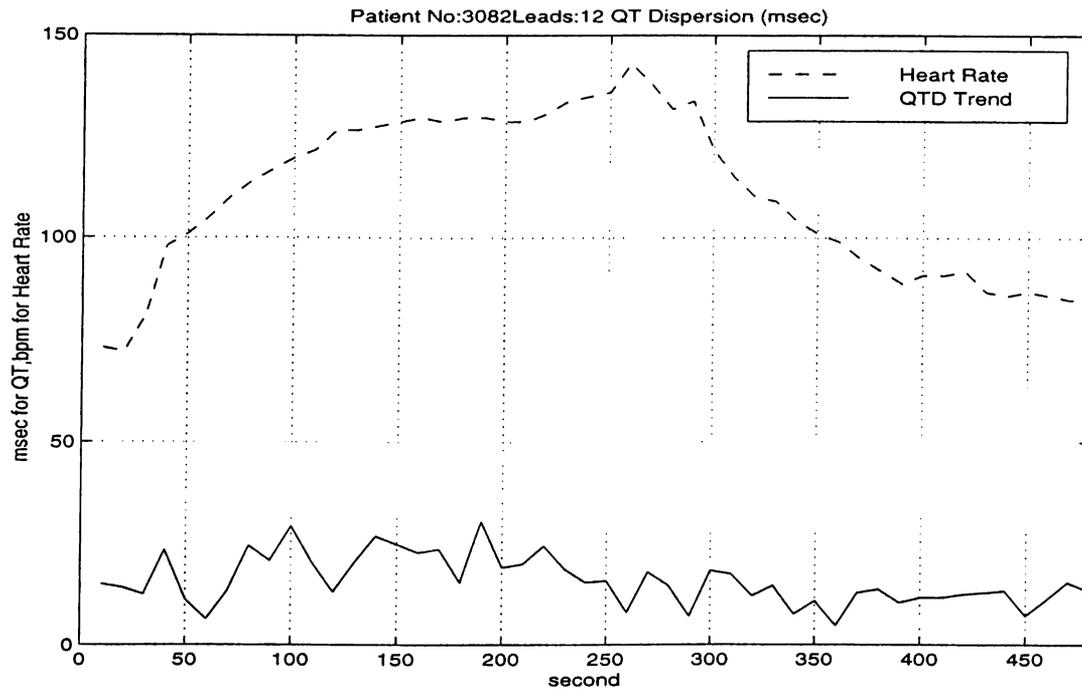


Figure A.18: QTD and Heart Rate for patient 3082 ST=- QT=- A=?

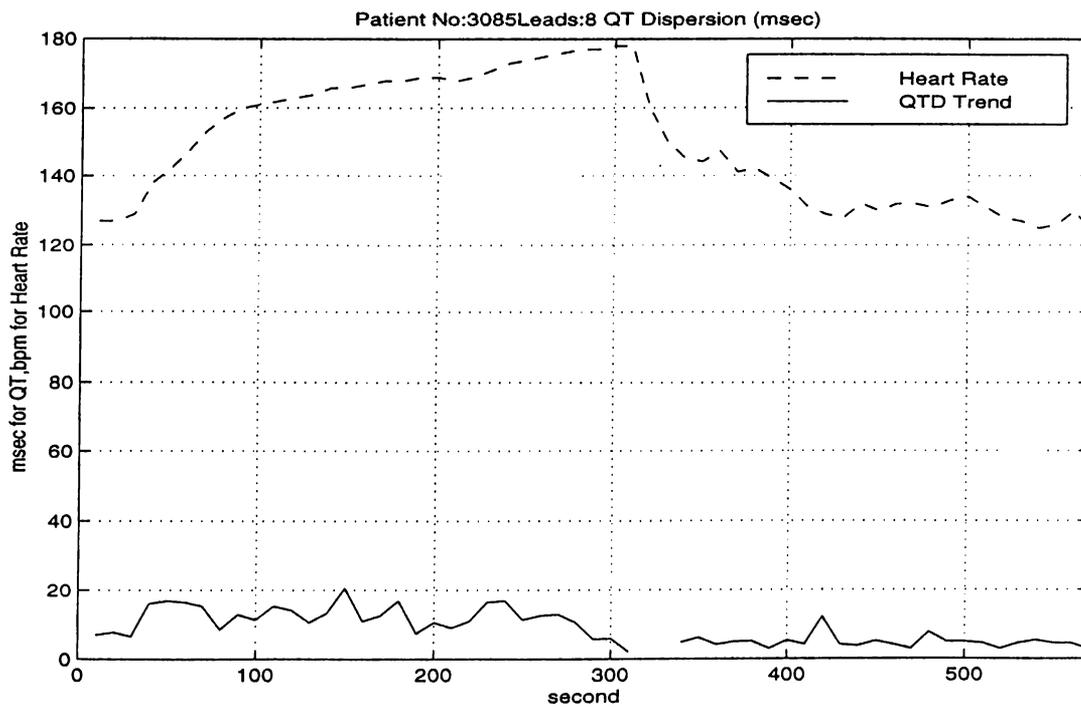


Figure A.19: QTD and Heart Rate for patient 3085 ST=- QT=- A=?

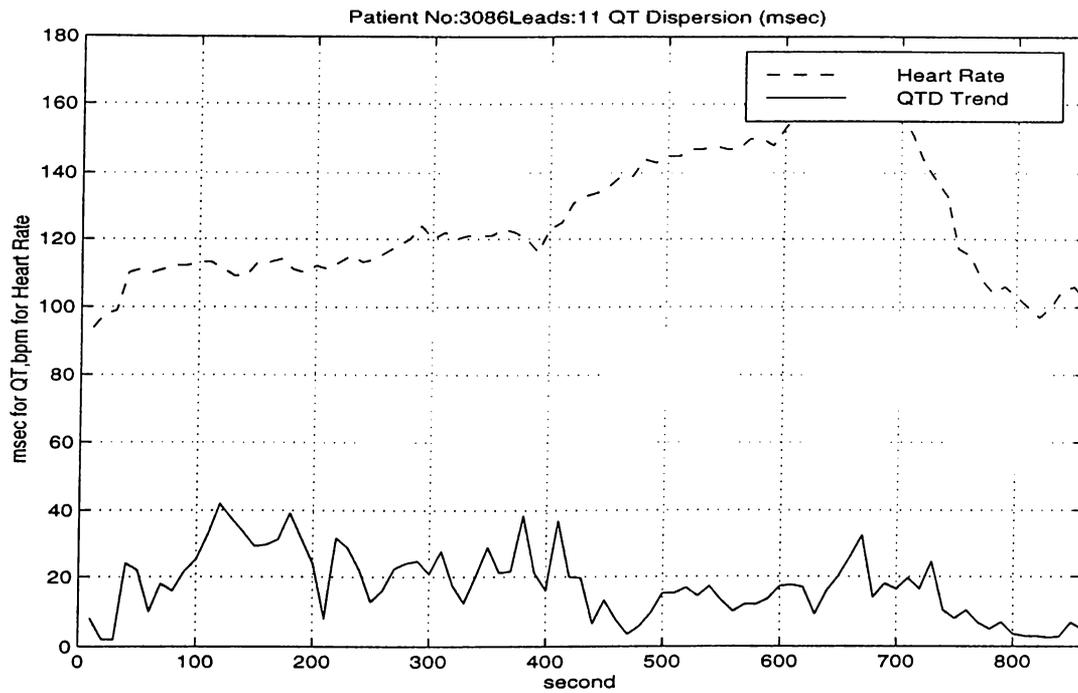


Figure A.20: QTD and Heart Rate for patient 3086 ST=- QT=- A=?

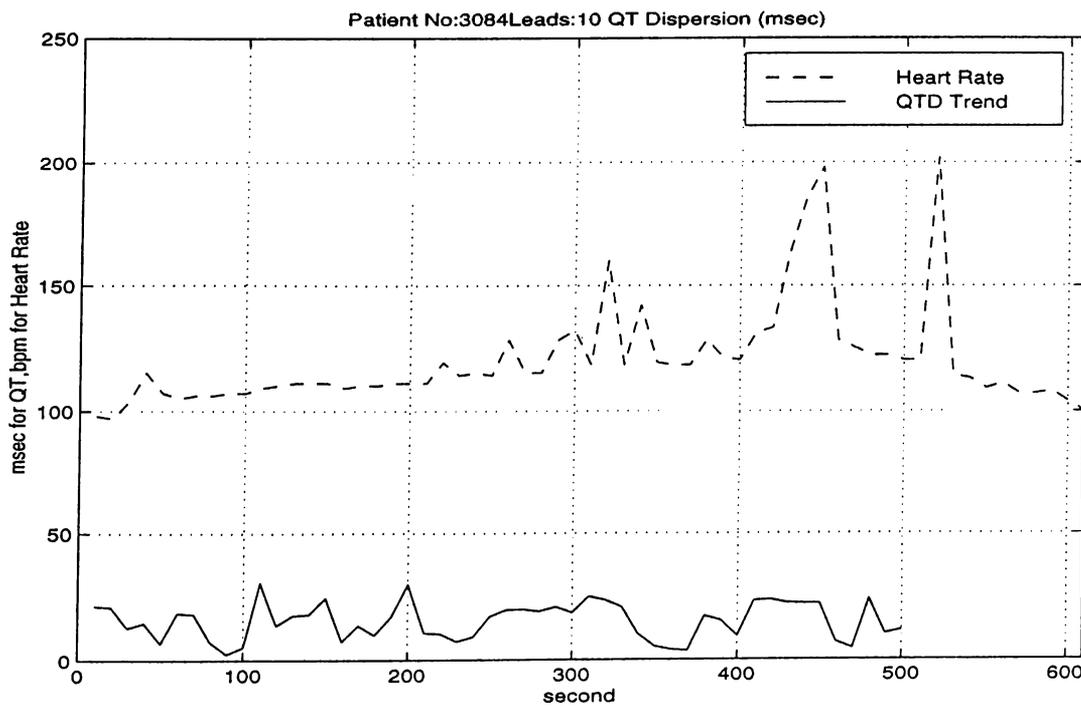


Figure A.21: QTD and Heart Rate for patient 3084 ST=- QT=- A=?

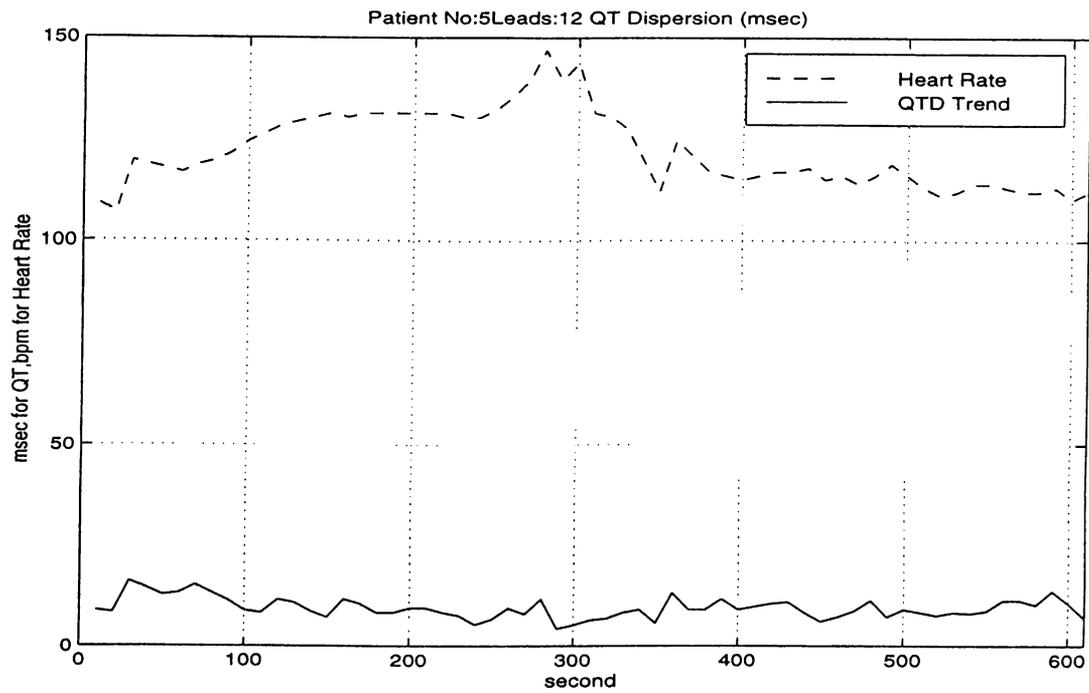


Figure A.22: QTD and Heart Rate for patient 5 ST=- QT=- A=?

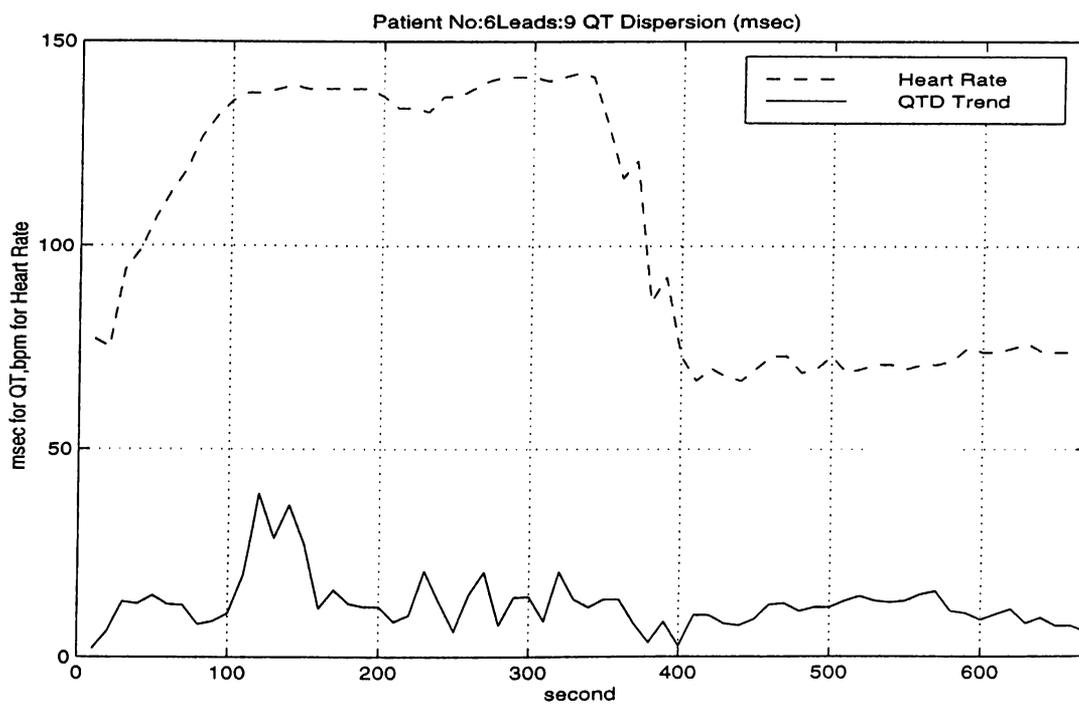


Figure A.23: QTD and Heart Rate for patient 6 ST=- QT=- A=?

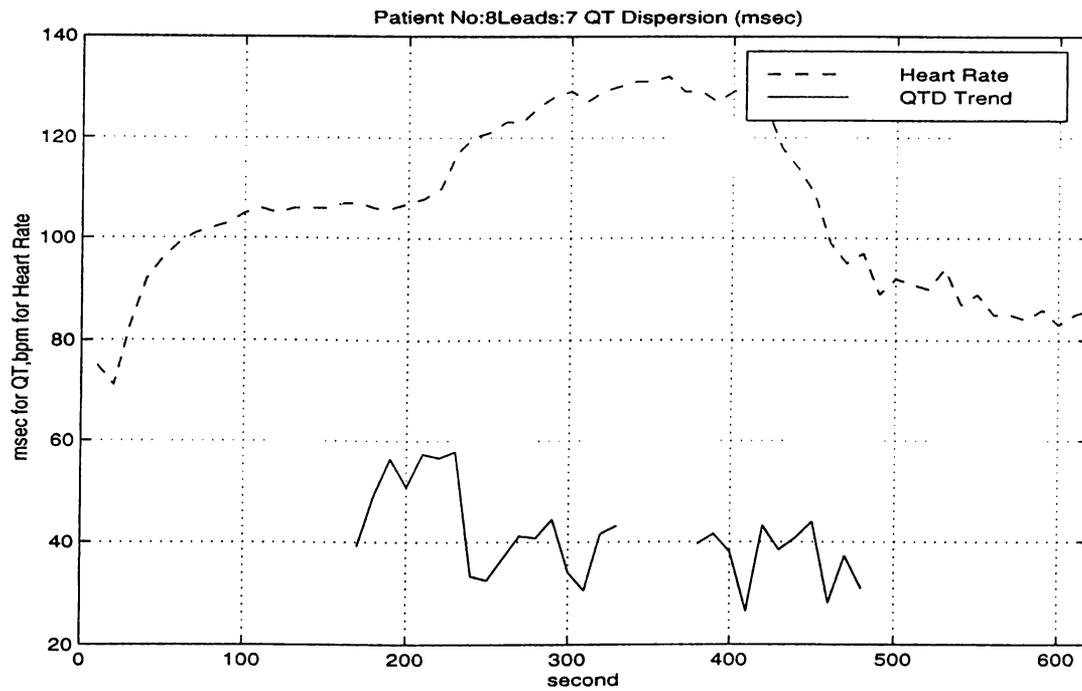


Figure A.24: QTD and Heart Rate for patient 8 ST=- QT=- A=?

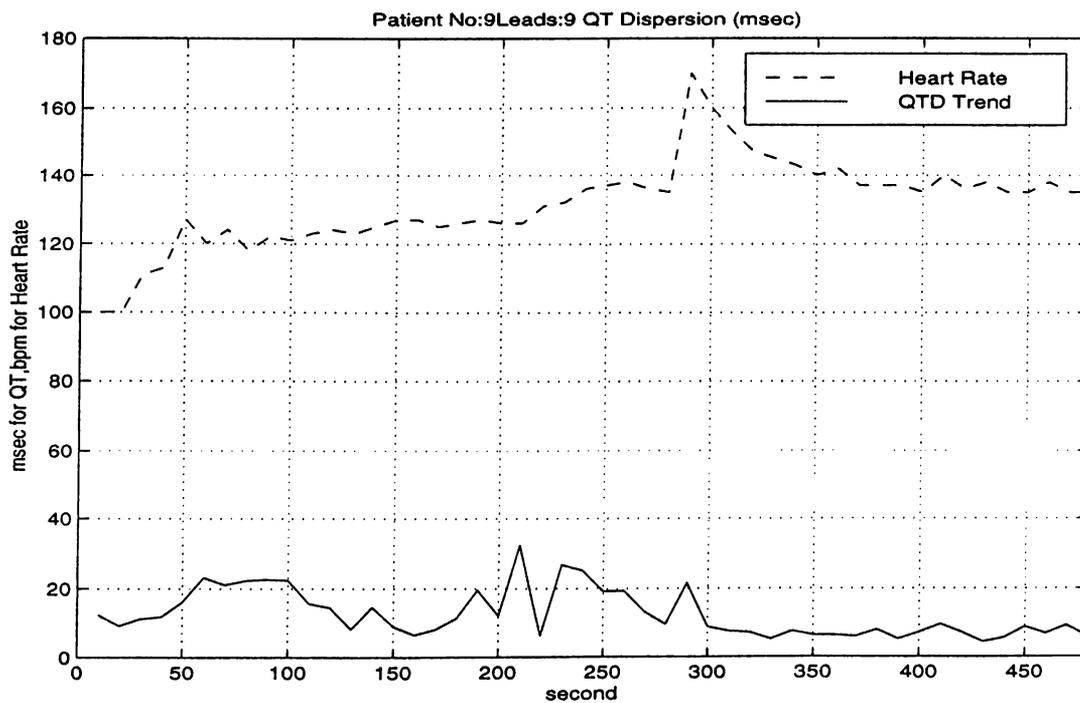


Figure A.25: QTD and Heart Rate for patient 9 ST=- QT=- A=?

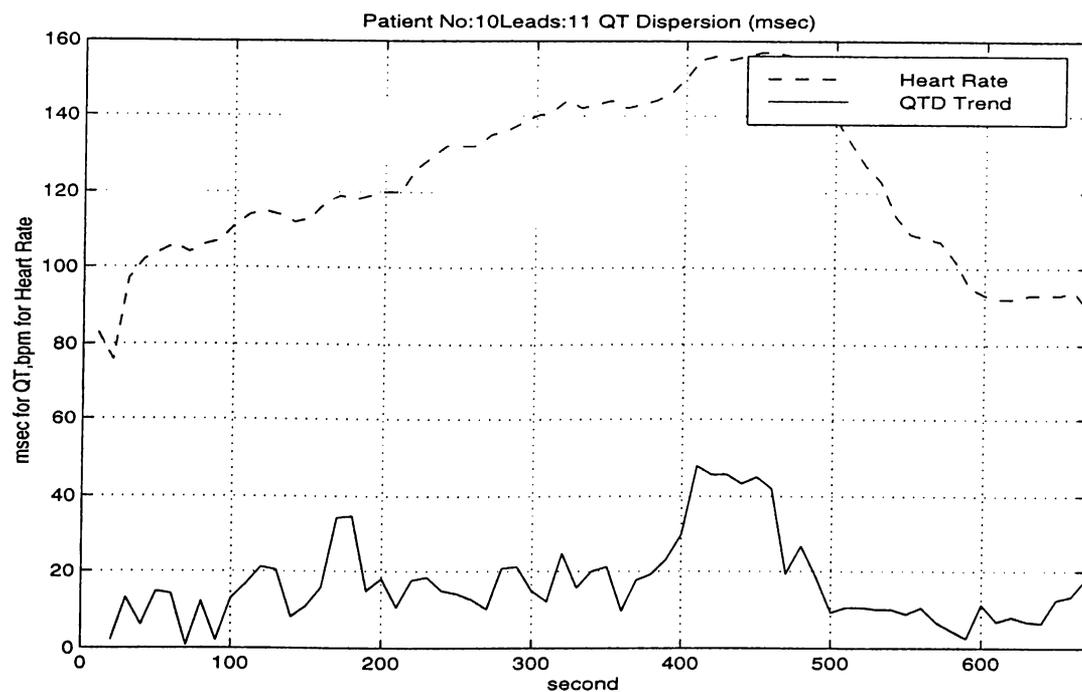


Figure A.26: QTD and Heart Rate for patient 10 ST=- QT=- A=?

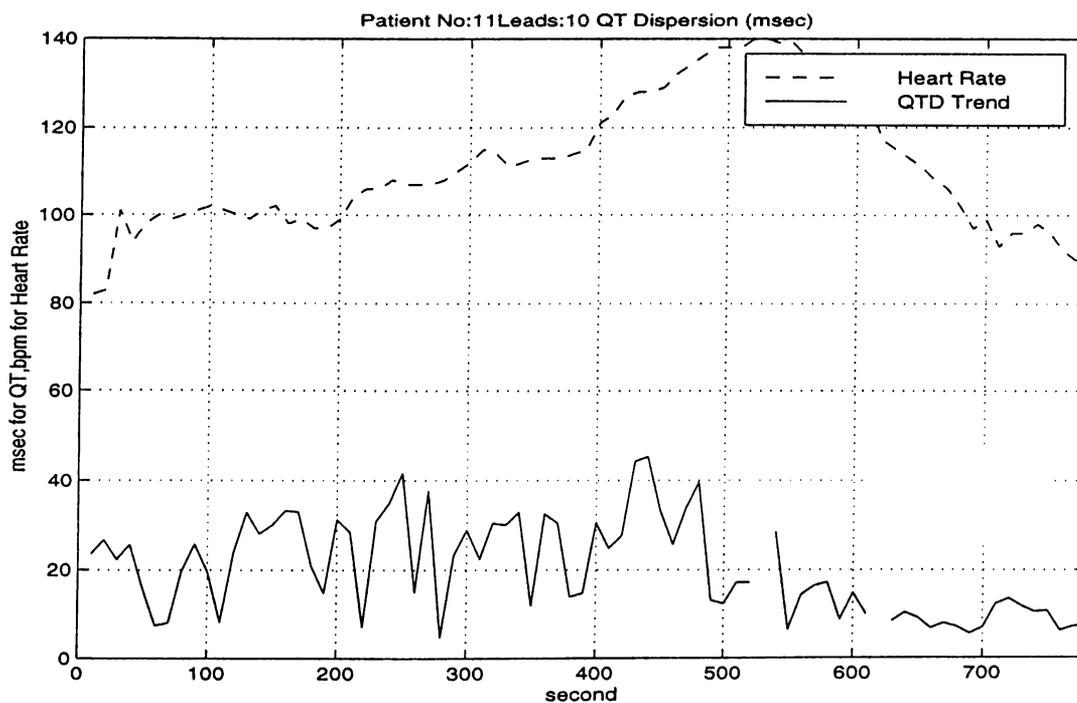


Figure A.27: QTD and Heart Rate for patient 11 ST=- QT=- A=?

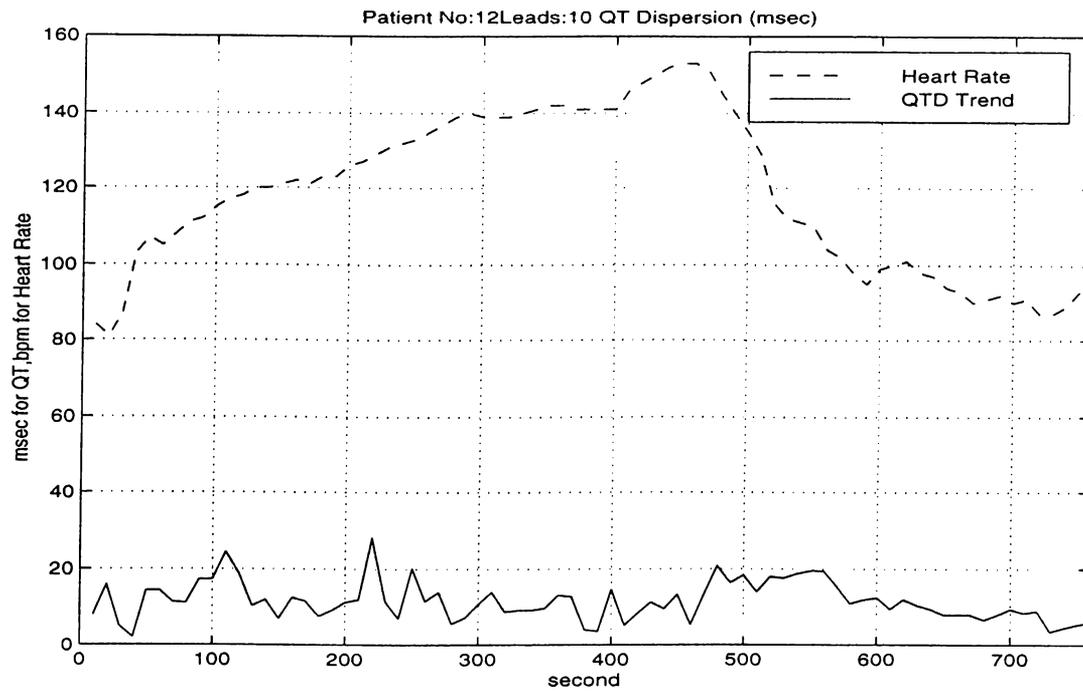


Figure A.28: QTD and Heart Rate for patient 12 ST-- QT-- A=?

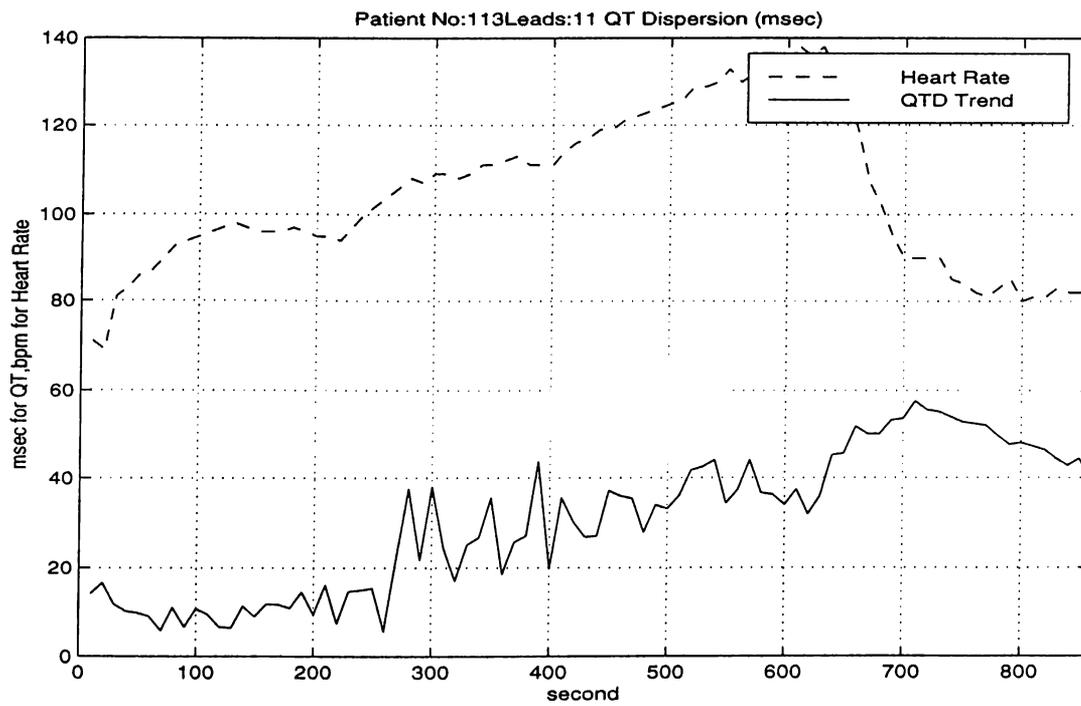


Figure A.29: QTD and Heart Rate for patient 113 ST-- QT-- A=?

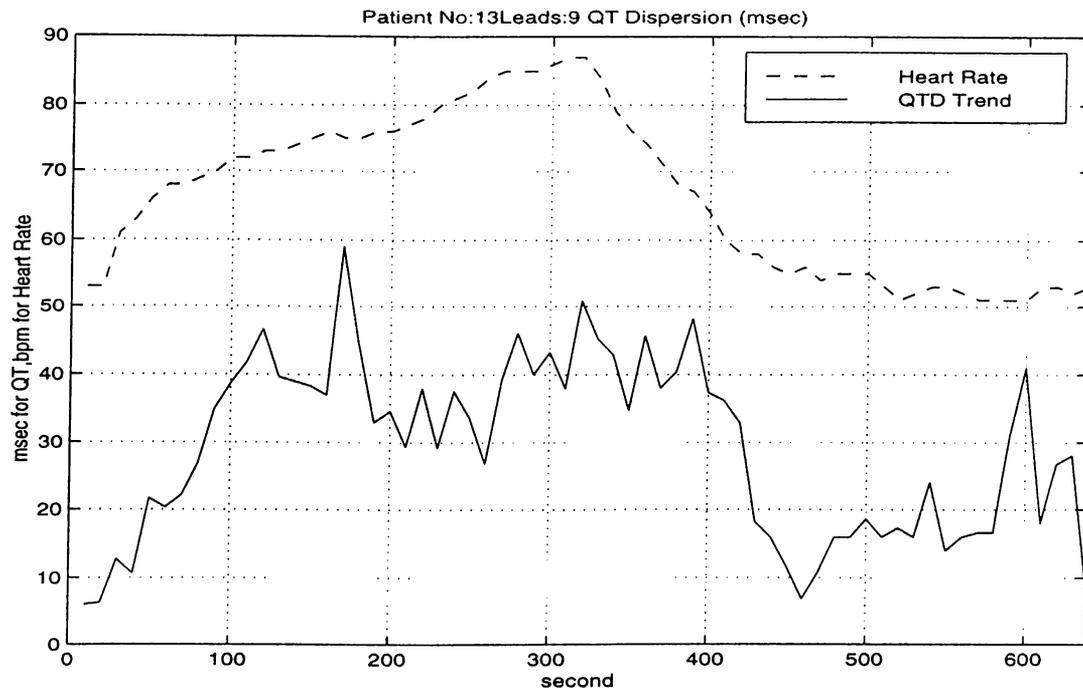


Figure A.30: QTD and Heart Rate for patient 13 ST=- QT=- A=?

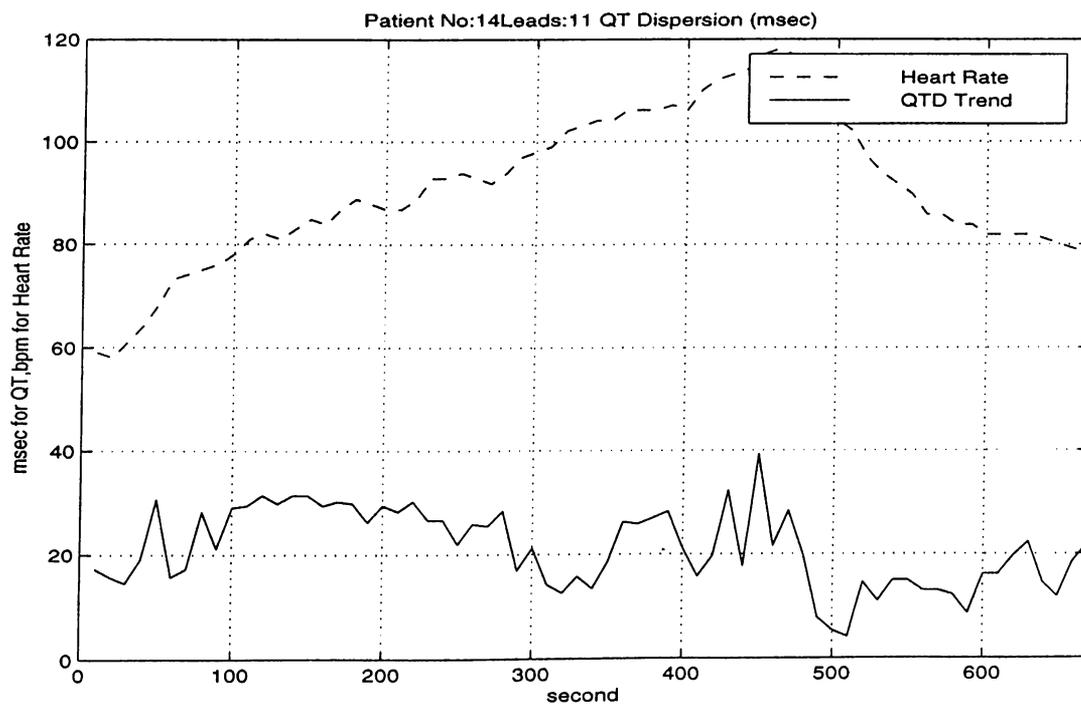


Figure A.31: QTD and Heart Rate for patient 14 ST=- QT=- A=?

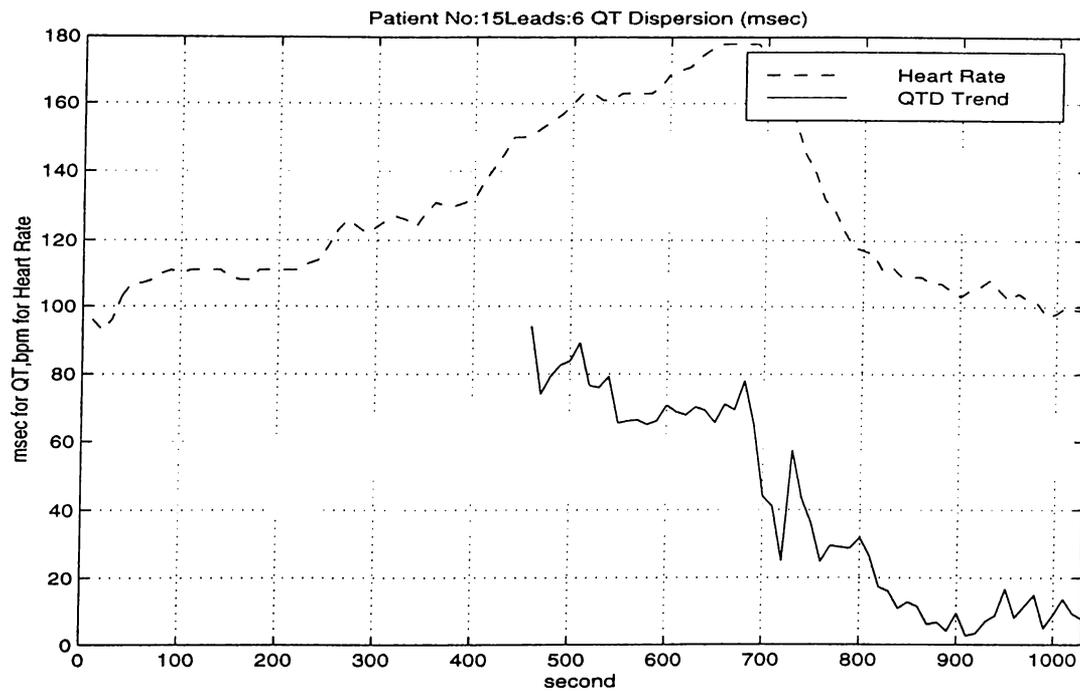


Figure A.32: QTD and Heart Rate for patient 15 ST=- QT=- A=?

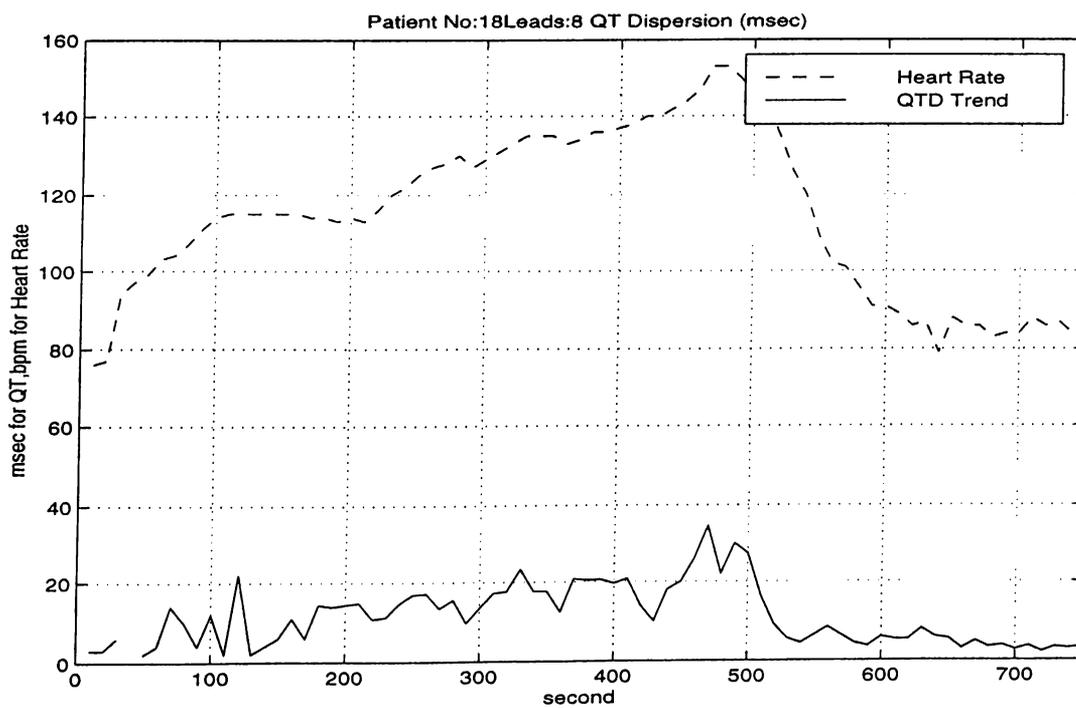


Figure A.33: QTD and Heart Rate for patient 18 ST=- QT=- A=?

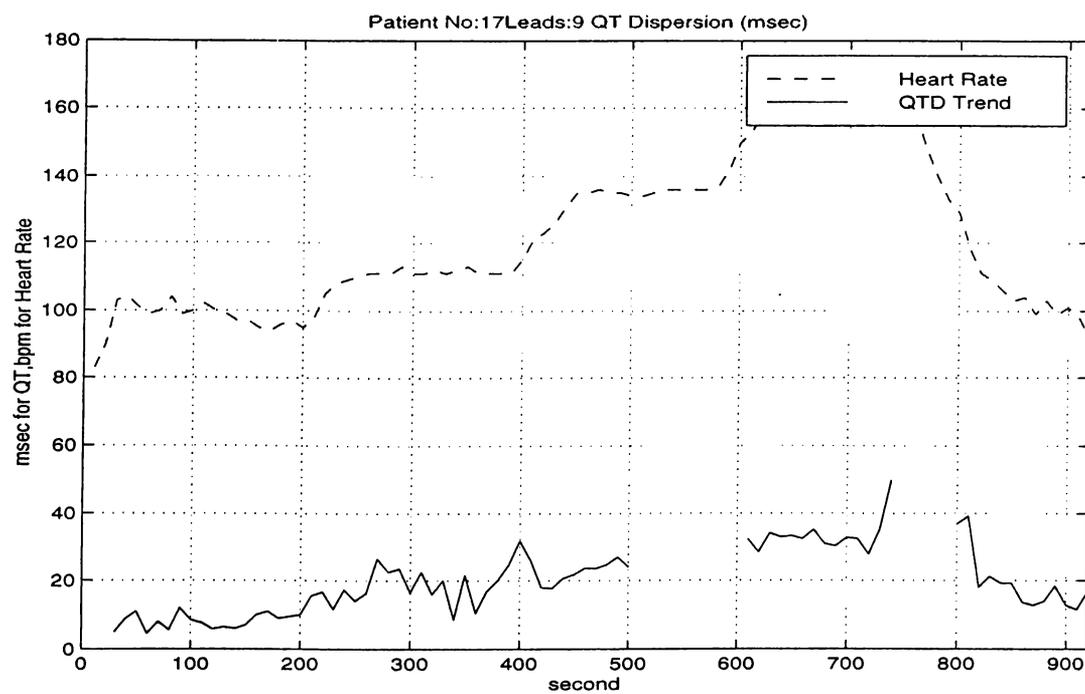


Figure A.34: QTD and Heart Rate for patient 17 ST=- QT=- A=?

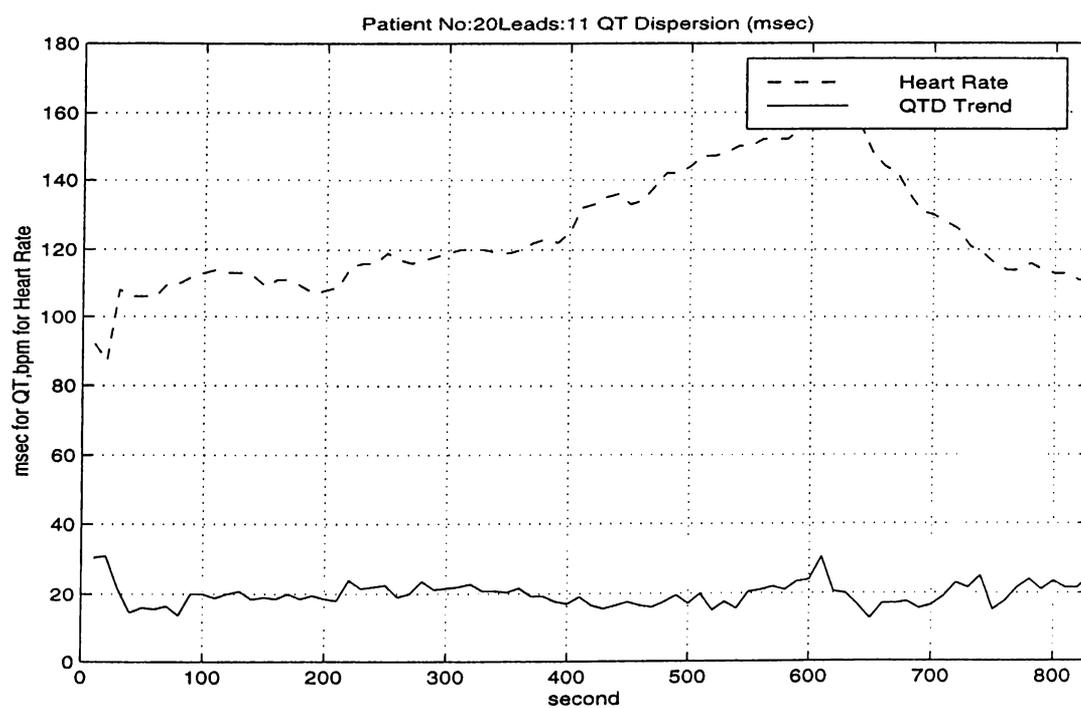


Figure A.35: QTD and Heart Rate for patient 20 ST=- QT=- A=?

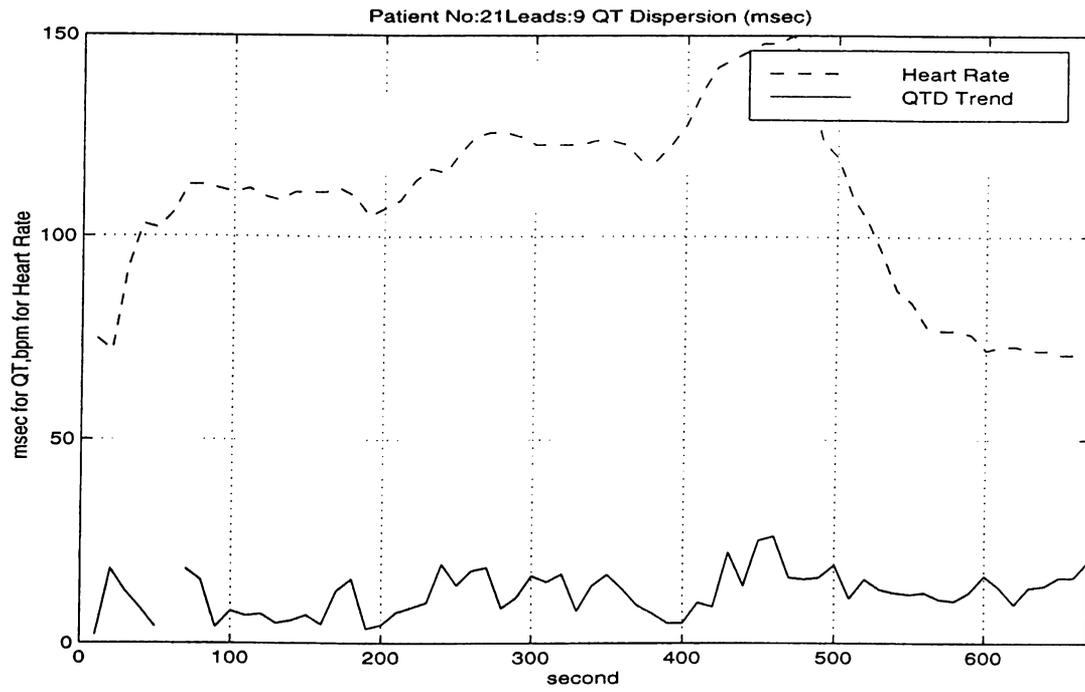


Figure A.36: QTD and Heart Rate for patient 21 ST=- QT=- A=?

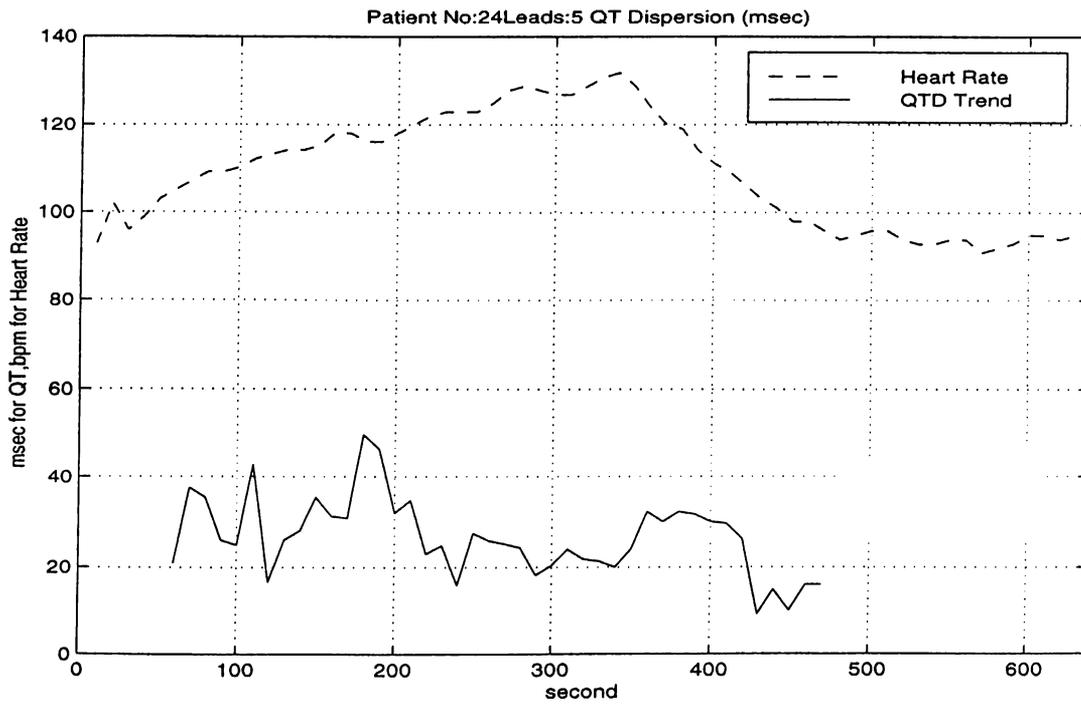


Figure A.37: QTD and Heart Rate for patient 24 ST=- QT=- A=?

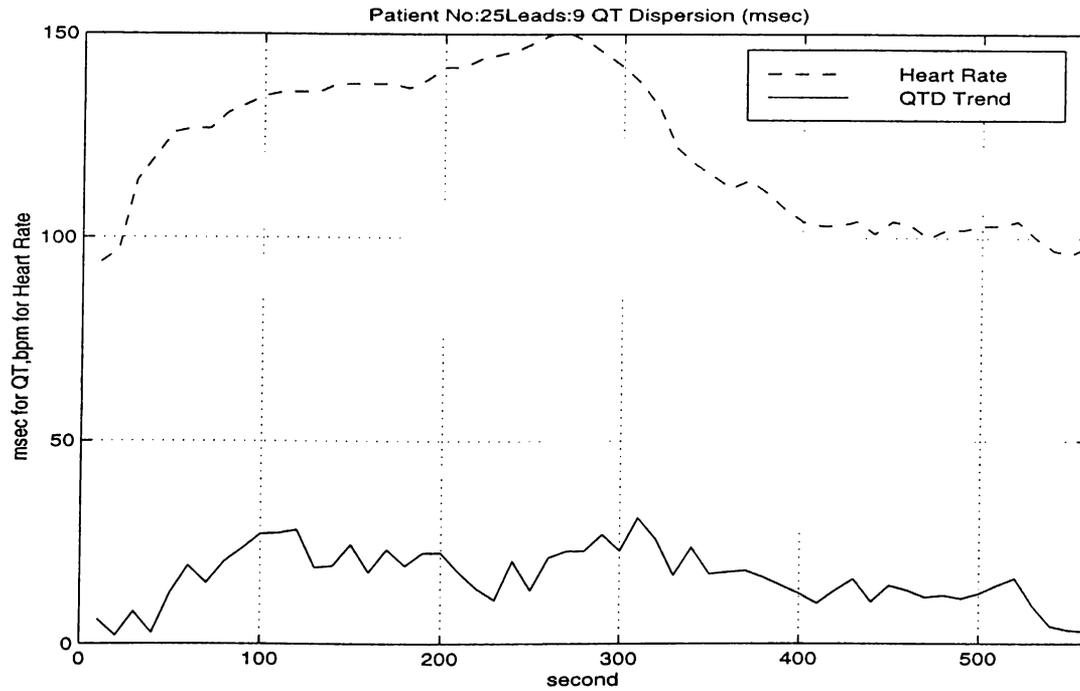


Figure A.38: QTD and Heart Rate for patient 25 ST=- QT=- A=?

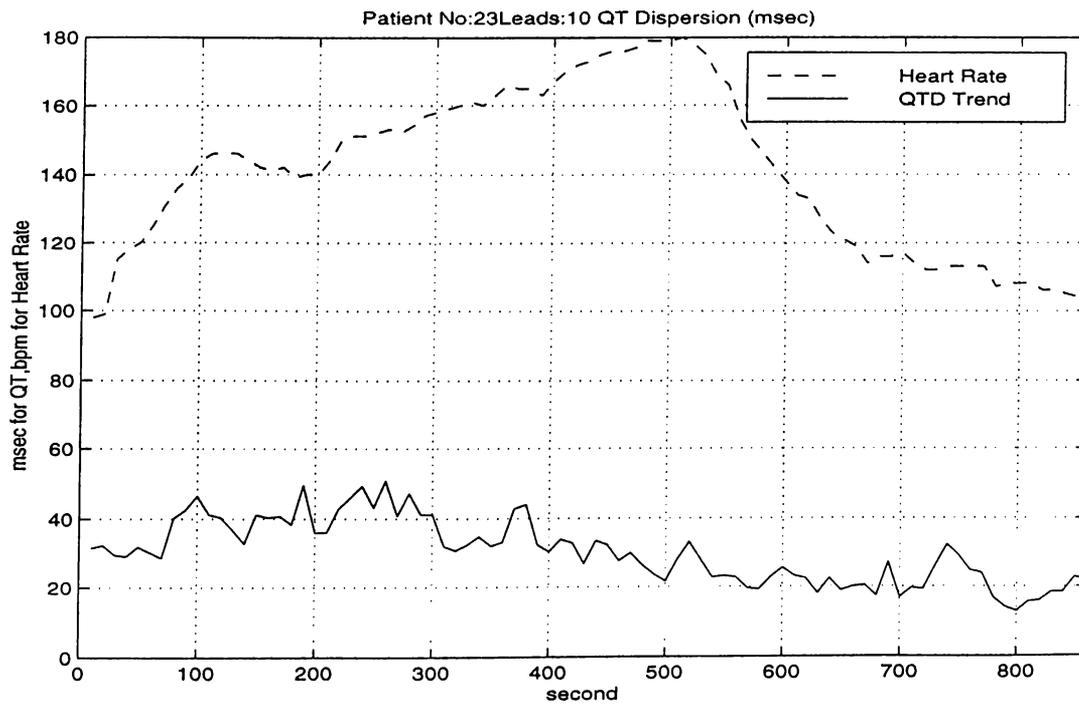


Figure A.39: QTD and Heart Rate for patient 23 ST=- QT=- A=?

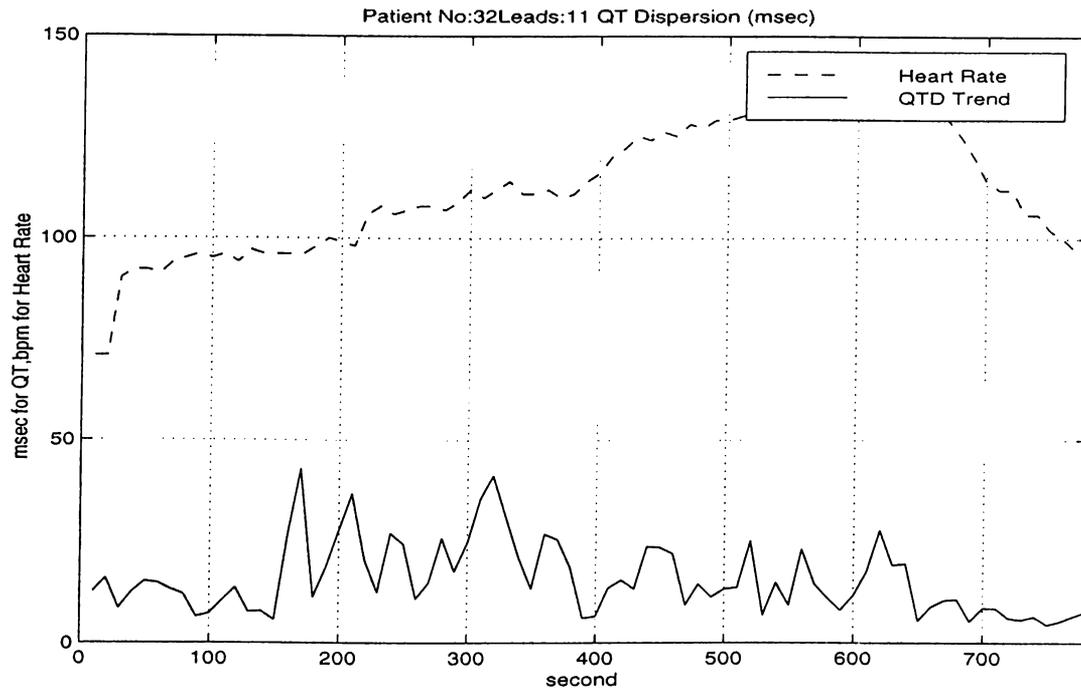


Figure A.40: QTD and Heart Rate for patient 32 ST=- QT=- A=?

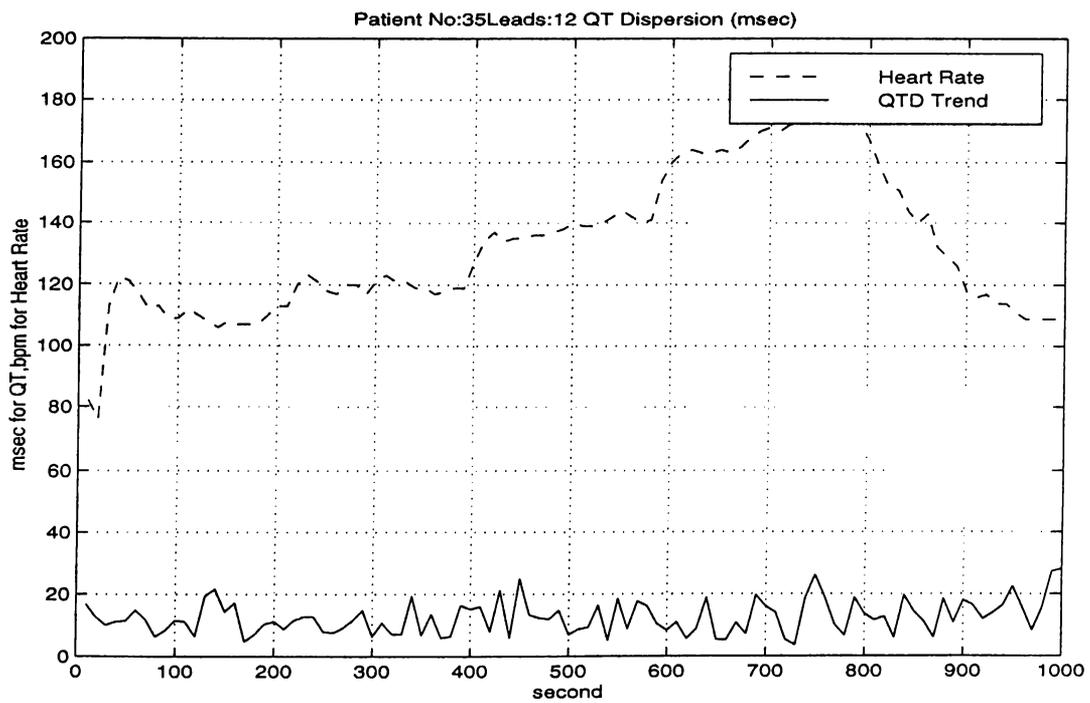


Figure A.41: QTD and Heart Rate for patient 35 ST=- QT=- A=?

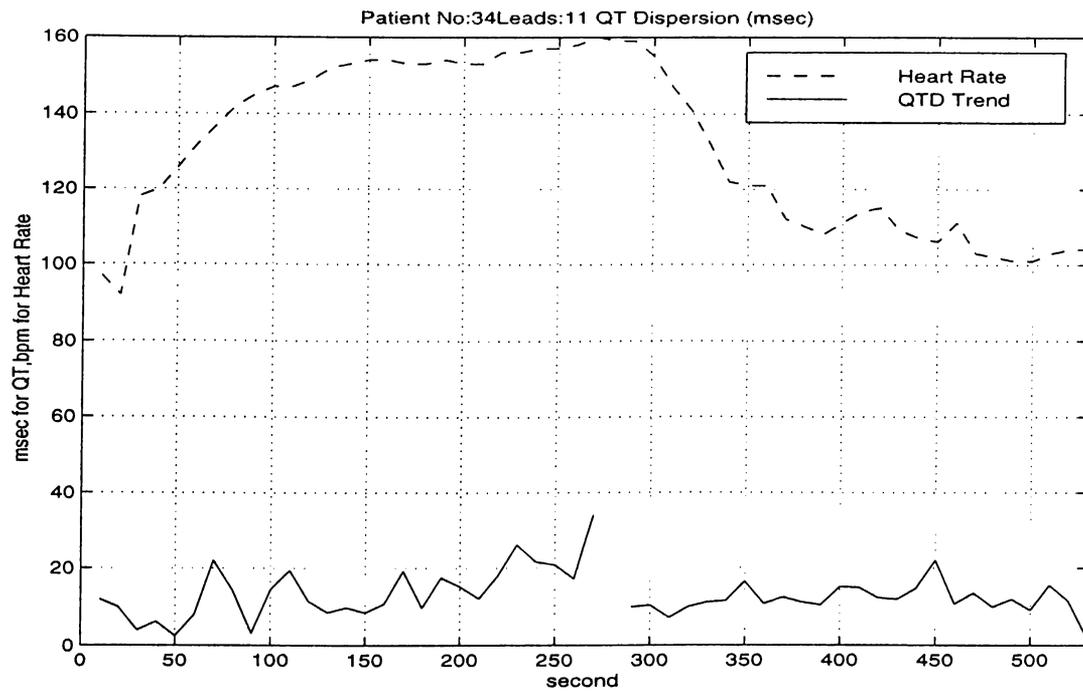


Figure A.42: QTD and Heart Rate for patient 34 ST=- QT=- A=?

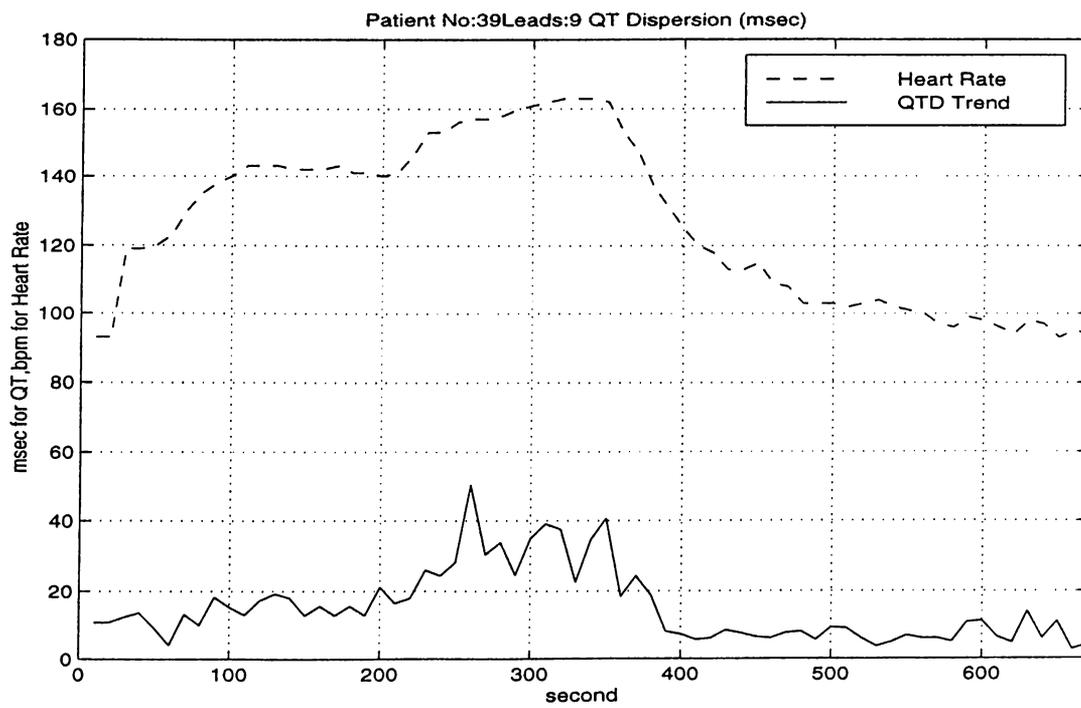


Figure A.43: QTD and Heart Rate for patient 39 ST=- QT=- A=?

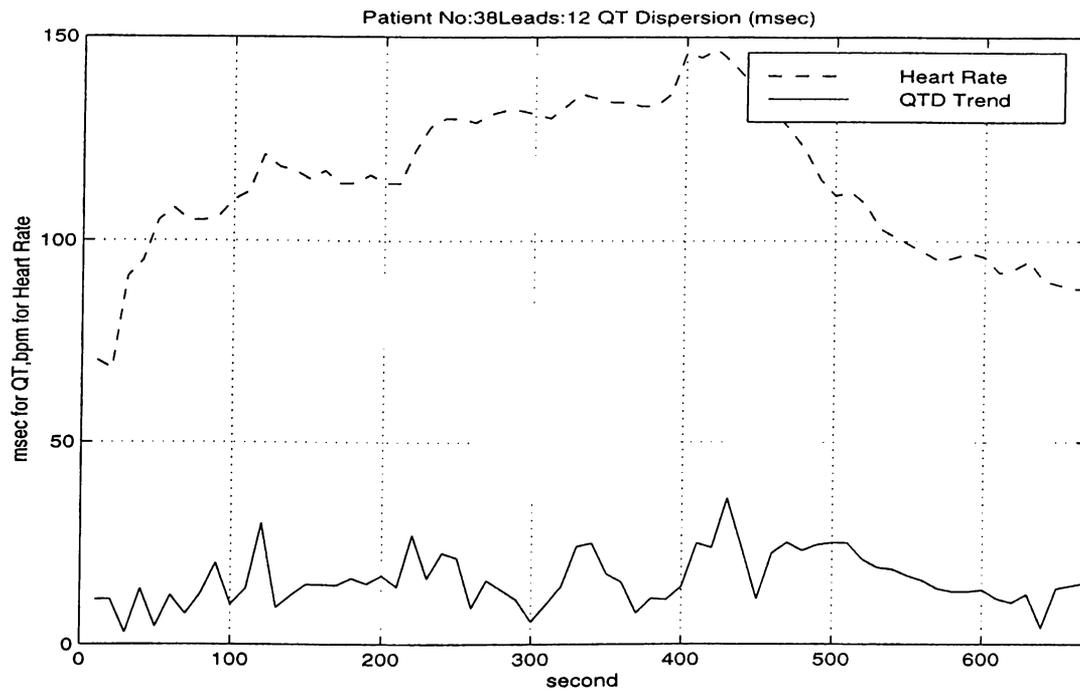


Figure A.44: QTD and Heart Rate for patient 38 ST=- QT=- A=?

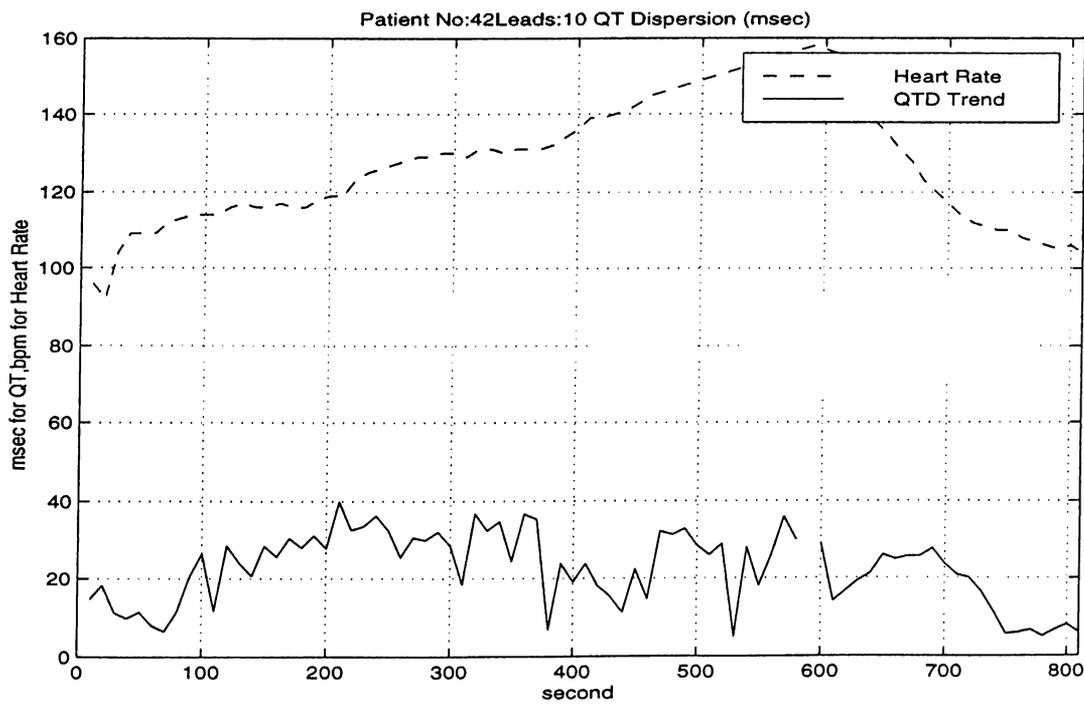


Figure A.45: QTD and Heart Rate for patient 42 ST=- QT=- A=?

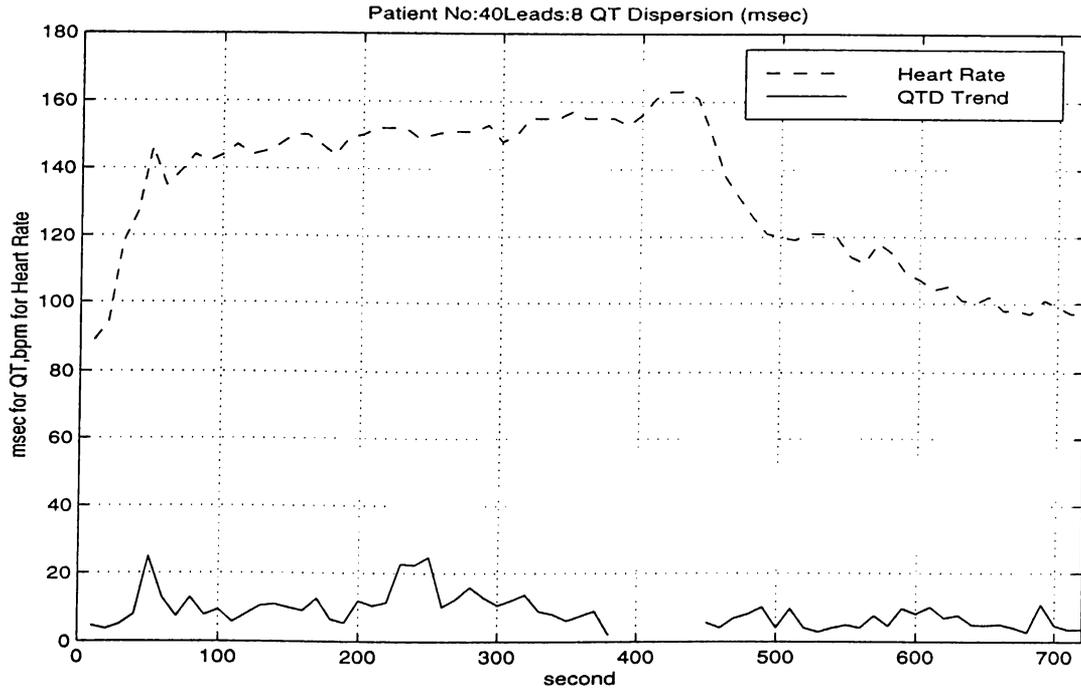


Figure A.46: QTD and Heart Rate for patient 40 ST=- QT=- A=?

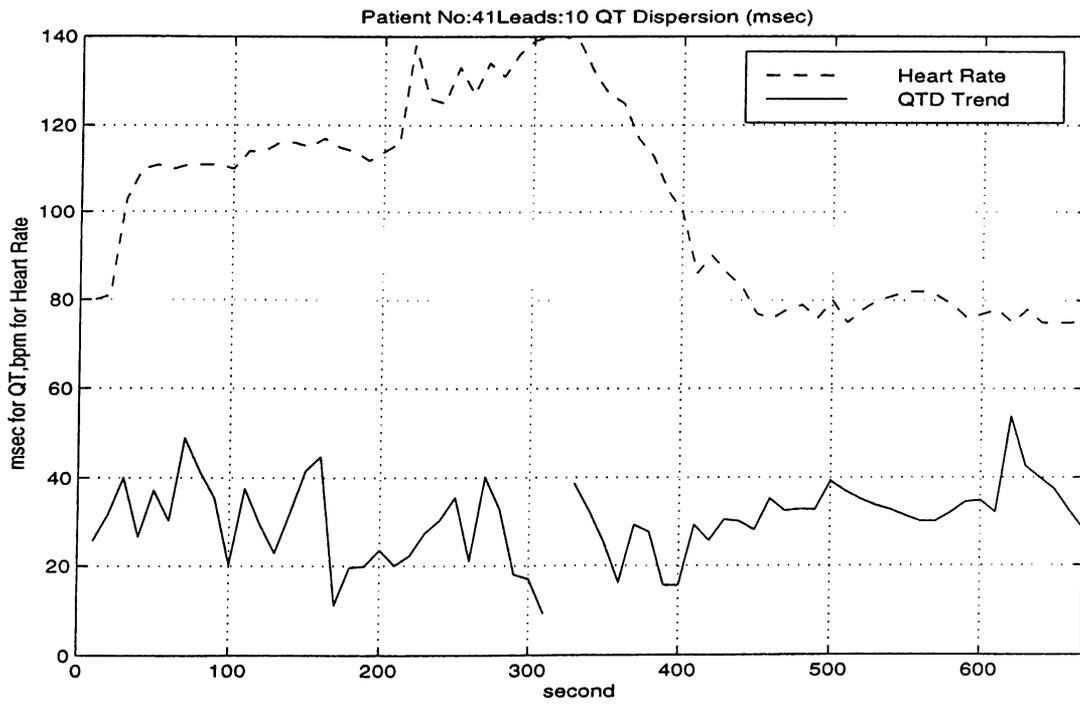


Figure A.47: QTD and Heart Rate for patient 41 ST=- QT=- A=?

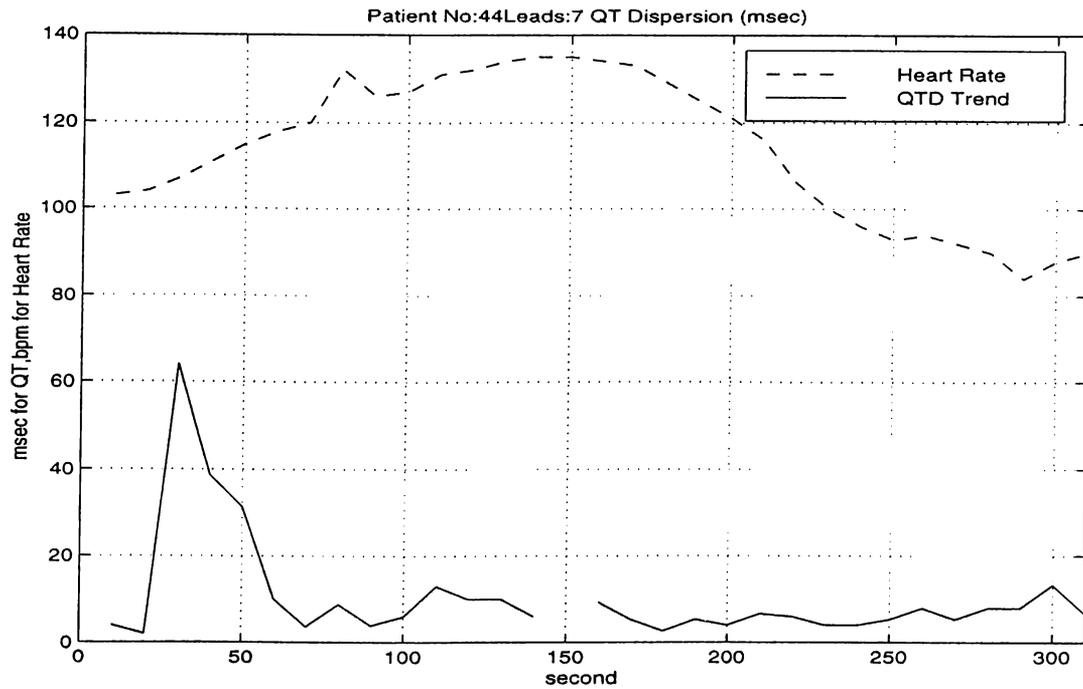


Figure A.48: QTD and Heart Rate for patient 44 ST=- QT=- A=?

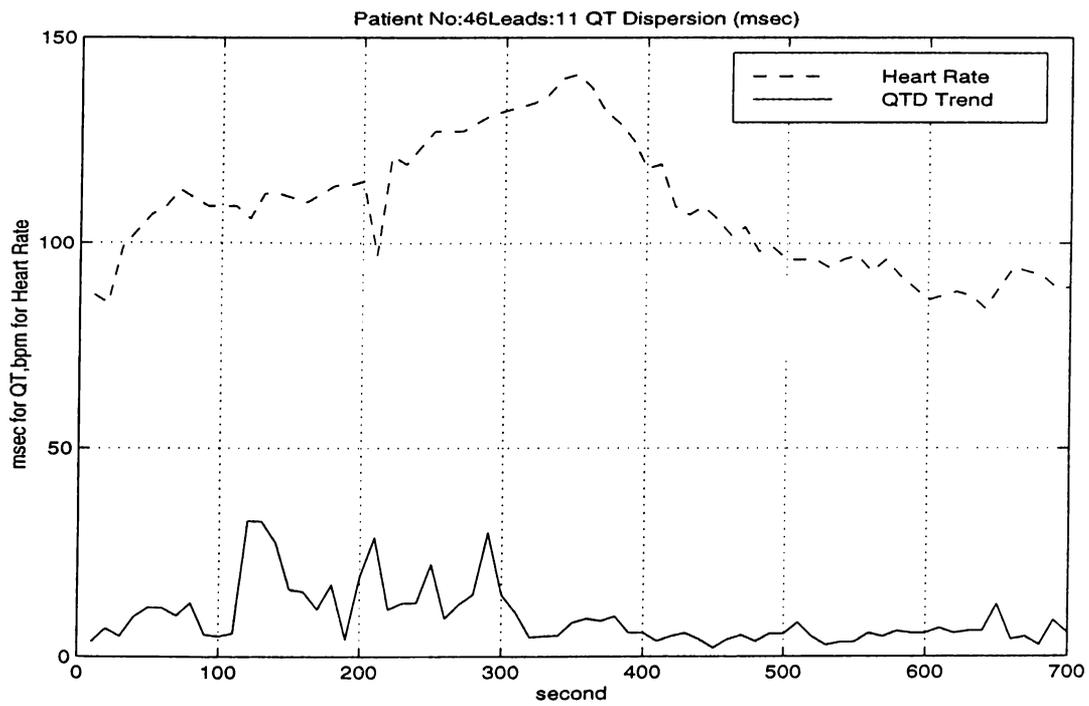


Figure A.49: QTD and Heart Rate for patient 46 ST=- QT=- A=?

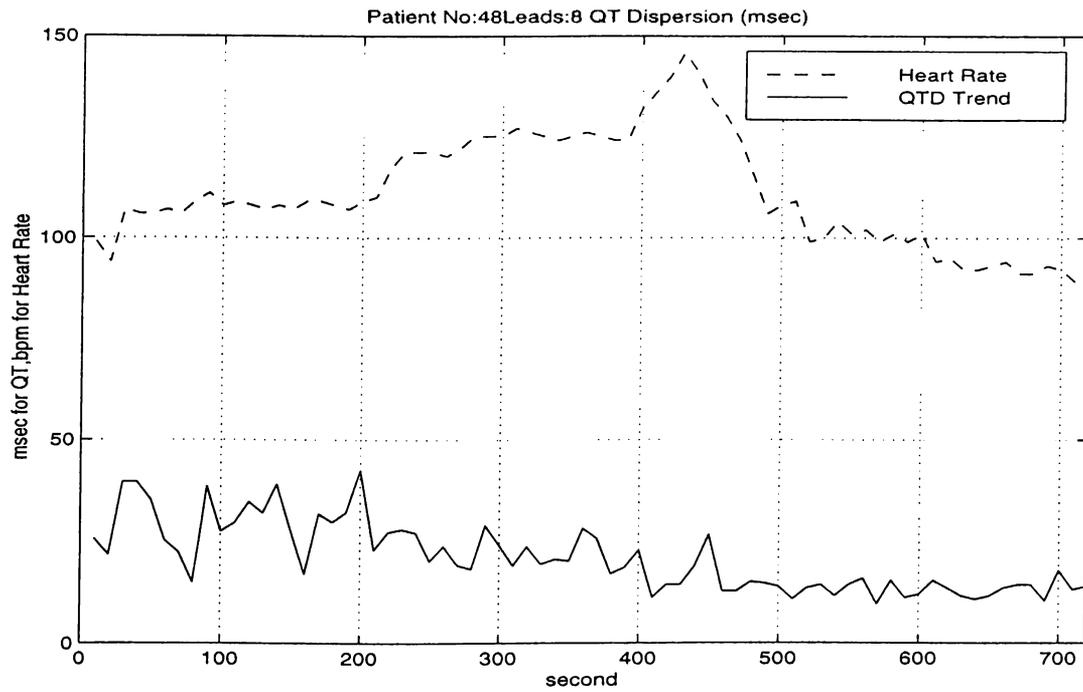


Figure A.50: QTD and Heart Rate for patient 48 ST=- QT=- A=?

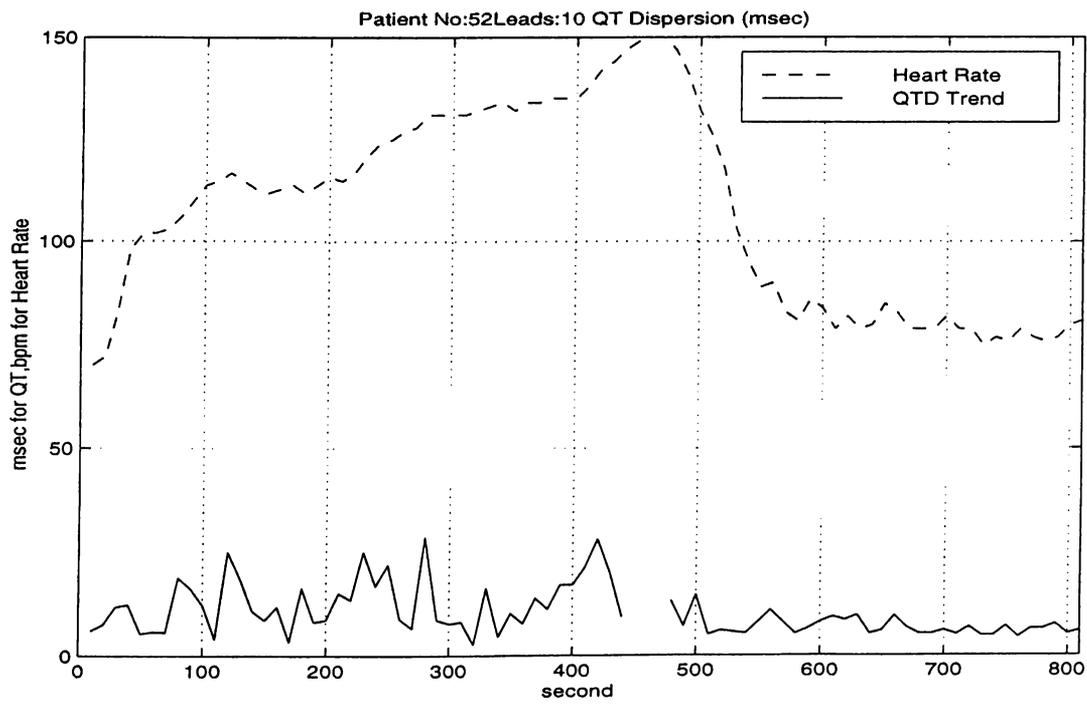


Figure A.51: QTD and Heart Rate for patient 52 ST=- QT=- A=?

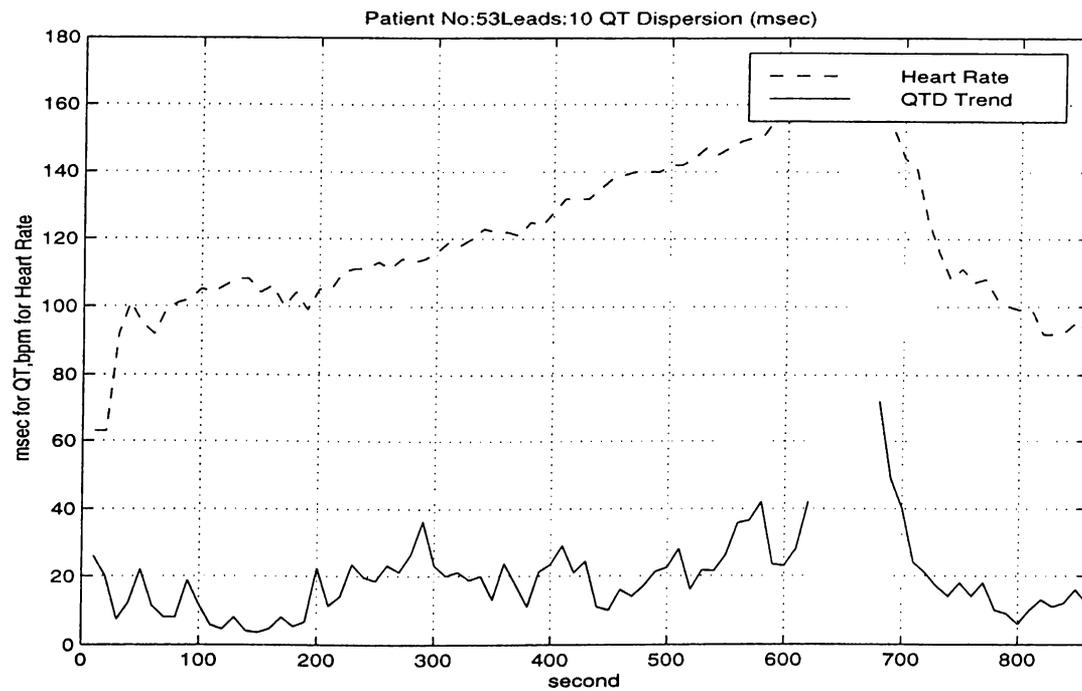


Figure A.52: QTD and Heart Rate for patient 53 ST=- QT=- A=?

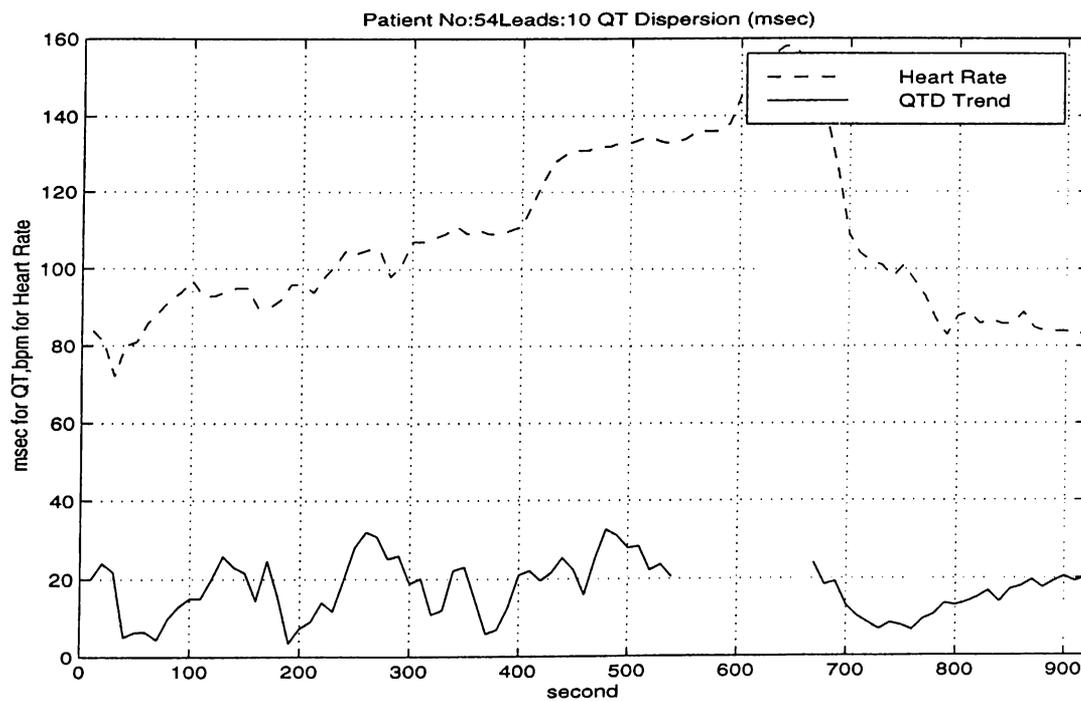


Figure A.53: QTD and Heart Rate for patient 54 ST=- QT=- A=?

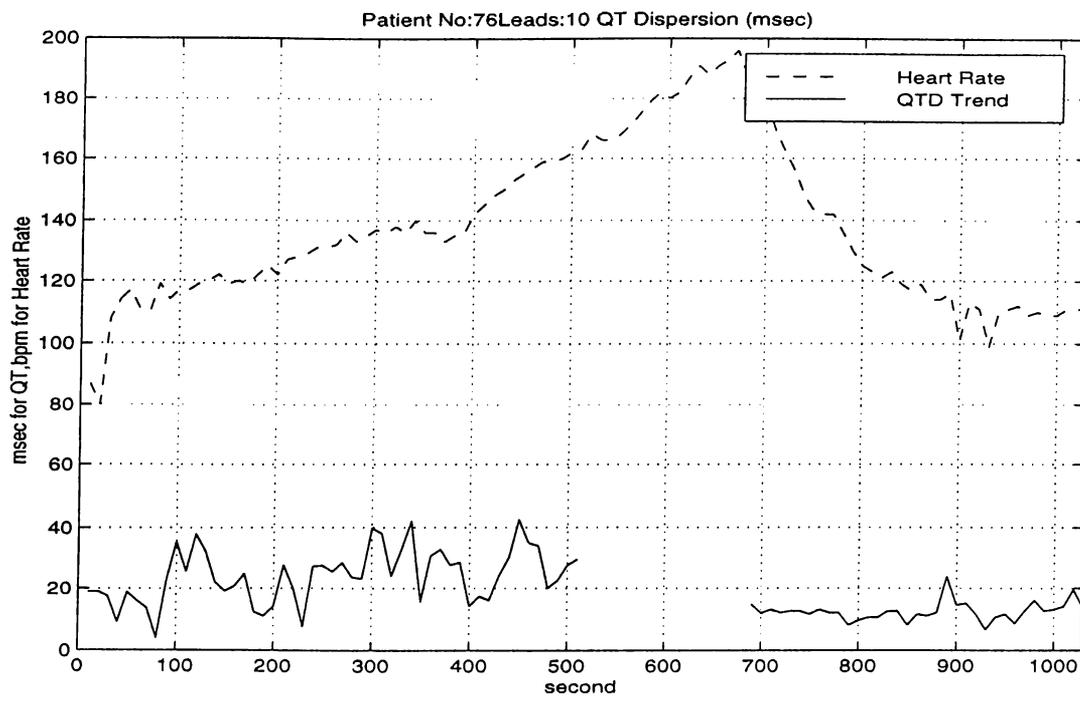


Figure A.54: QTD and Heart Rate for patient 76 ST=- QT=- A=?

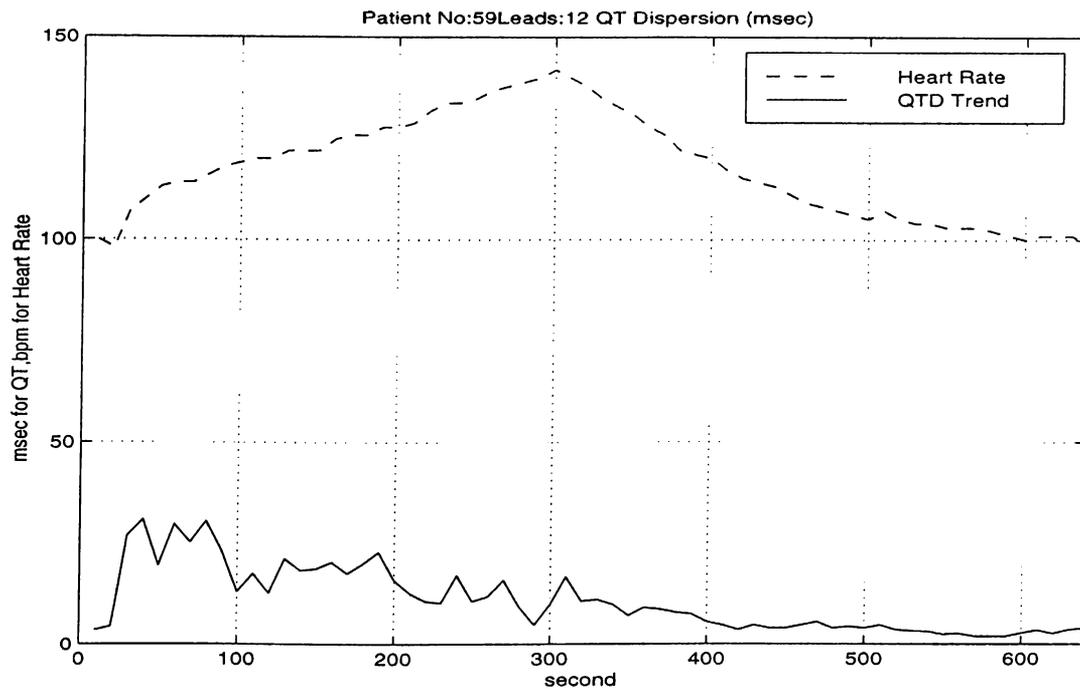


Figure A.55: QTD and Heart Rate for patient 59 ST=- QT=- A=?

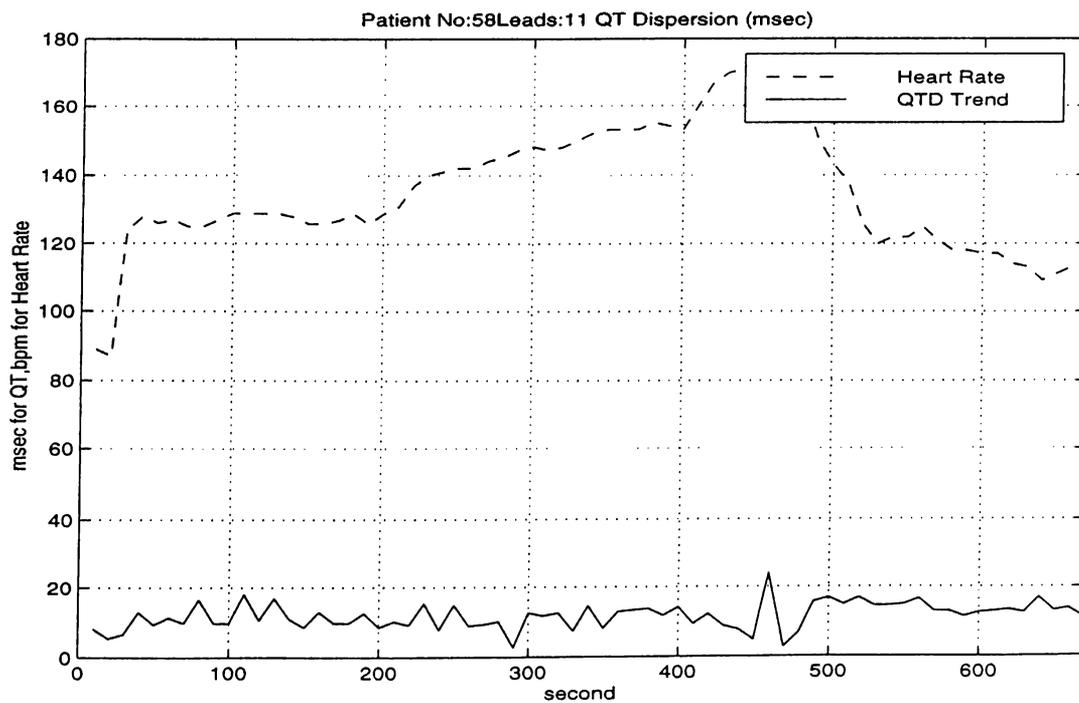


Figure A.56: QTD and Heart Rate for patient 58 ST=- QT=- A=?

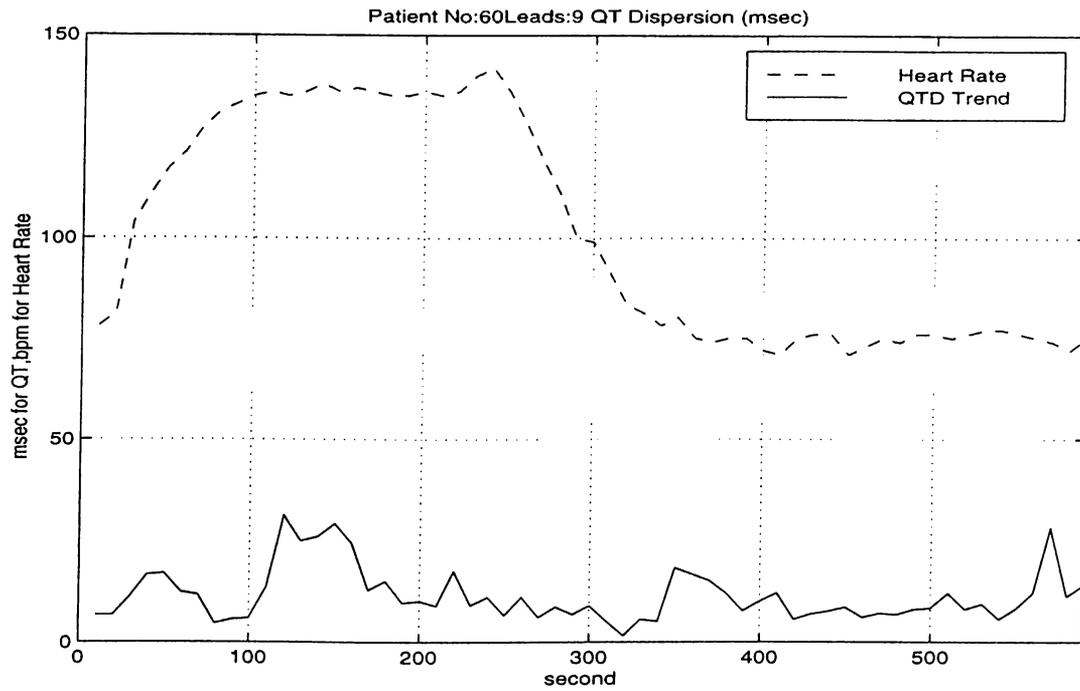


Figure A.57: QTD and Heart Rate for patient 60 ST=- QT=- A=?

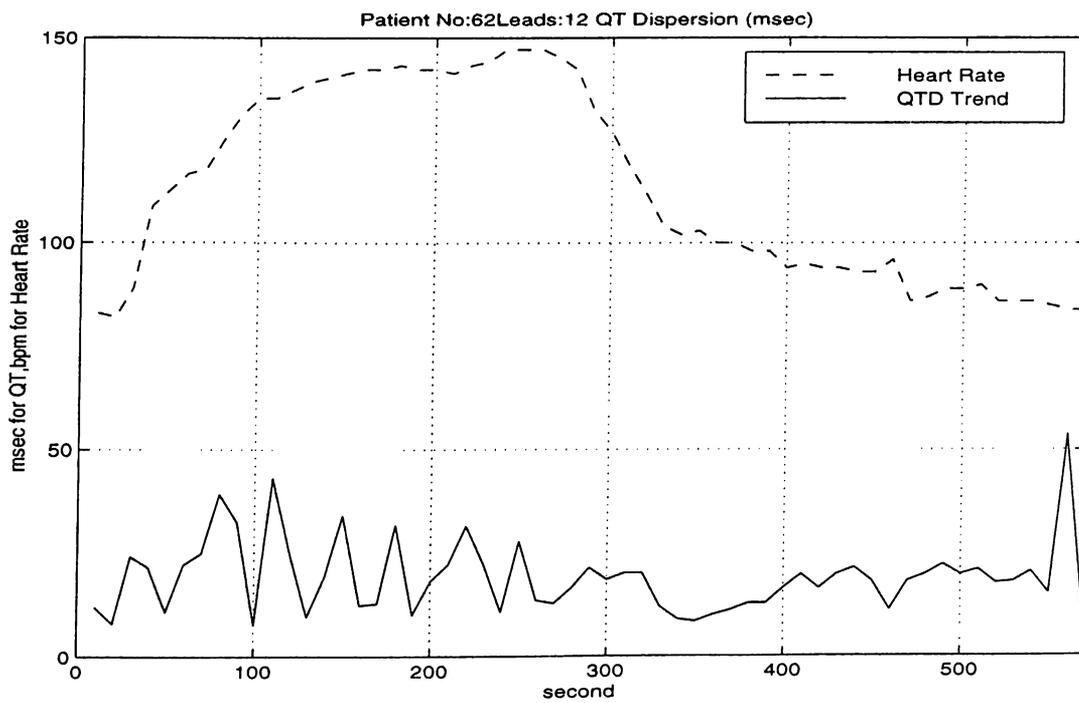


Figure A.58: QTD and Heart Rate for patient 62 ST=- QT=- A=?

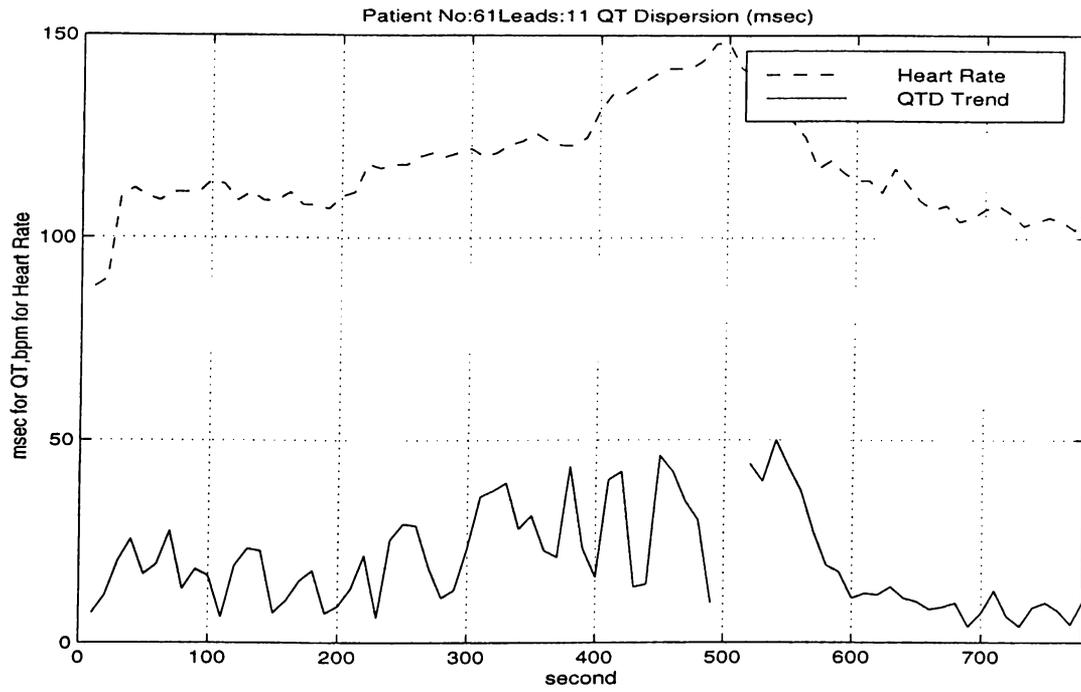


Figure A.59: QTD and Heart Rate for patient 61 ST=- QT=- A=?

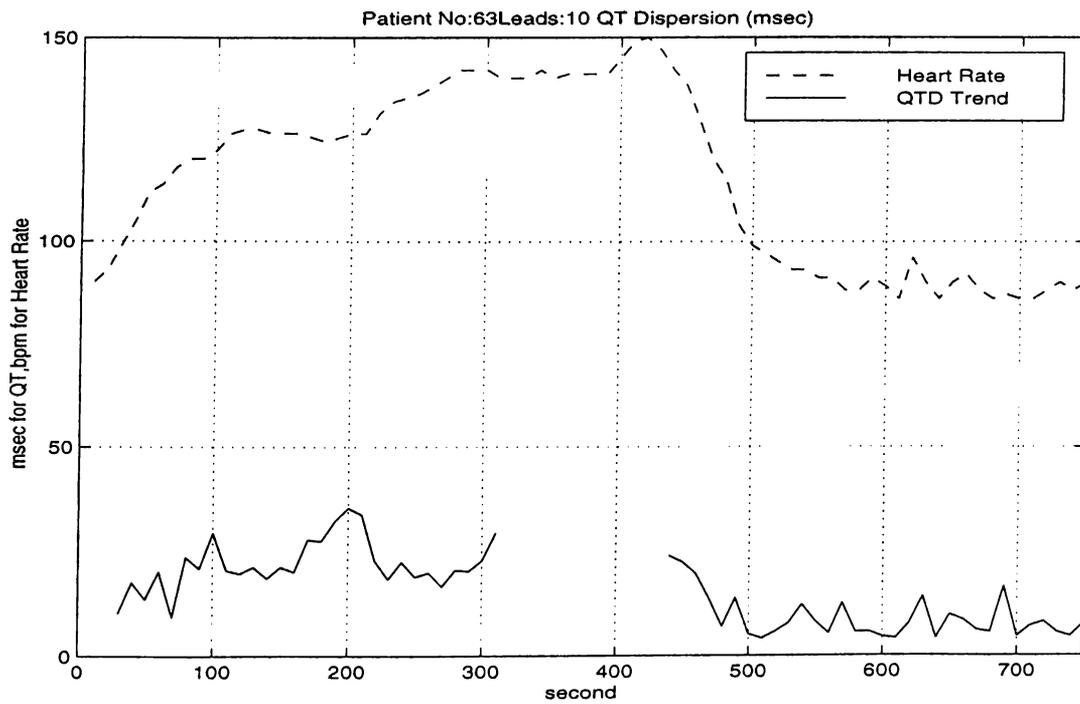


Figure A.60: QTD and Heart Rate for patient 63 ST=- QT=- A=?

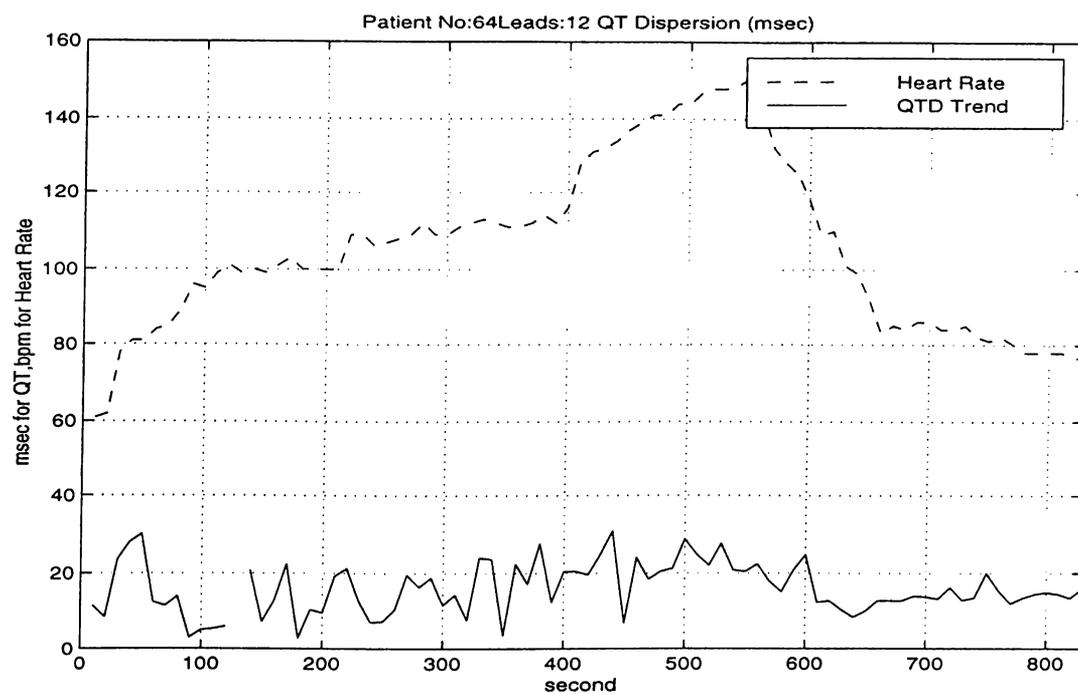


Figure A.61: QTD and Heart Rate for patient 64 ST=- QT=- A=?

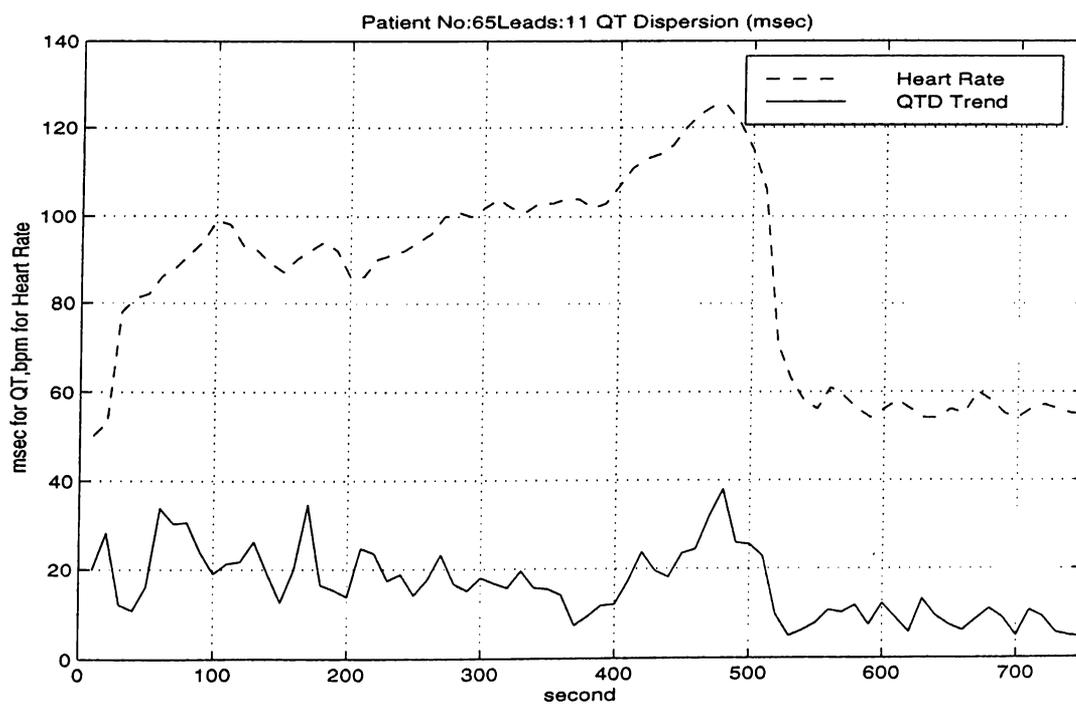


Figure A.62: QTD and Heart Rate for patient 65 ST=- QT=- A=?

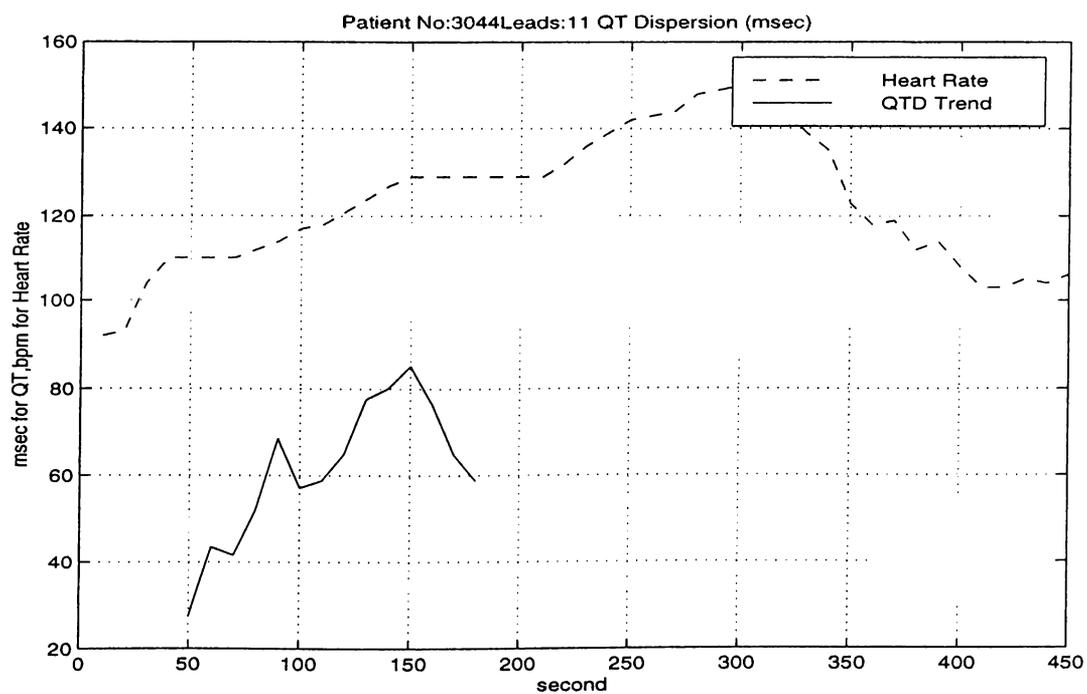


Figure A.63: QTD and Heart Rate for patient 3044 ST=+ QT=+ A=+

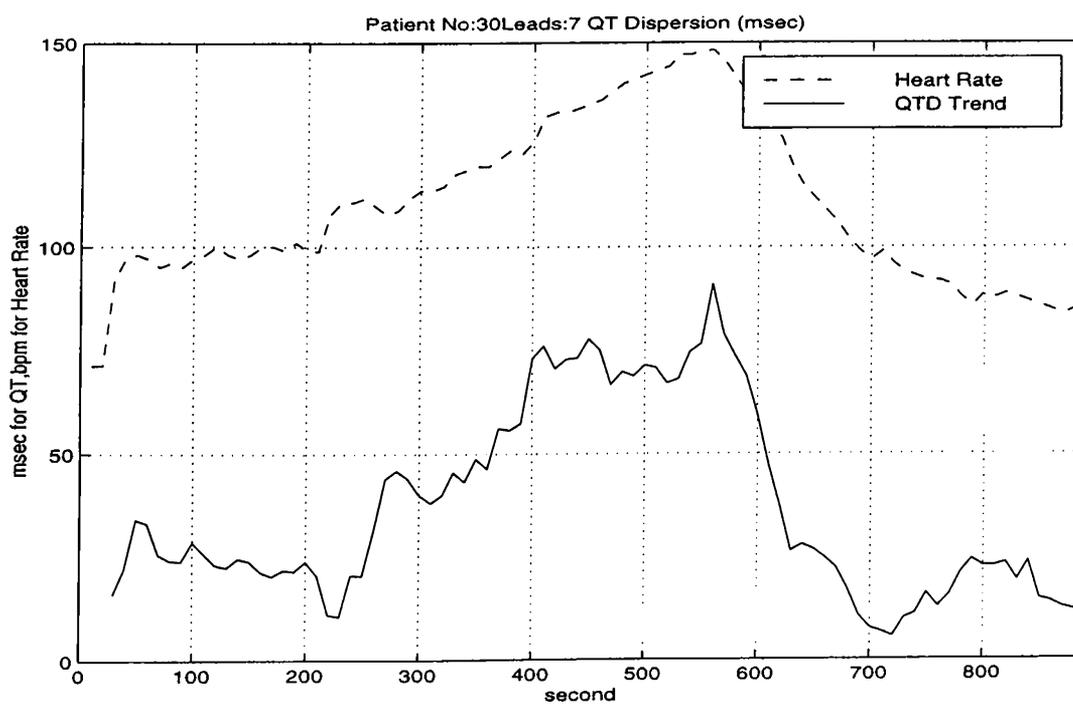


Figure A.64: QTD and Heart Rate for patient 30 ST=+ QT=+ A=+

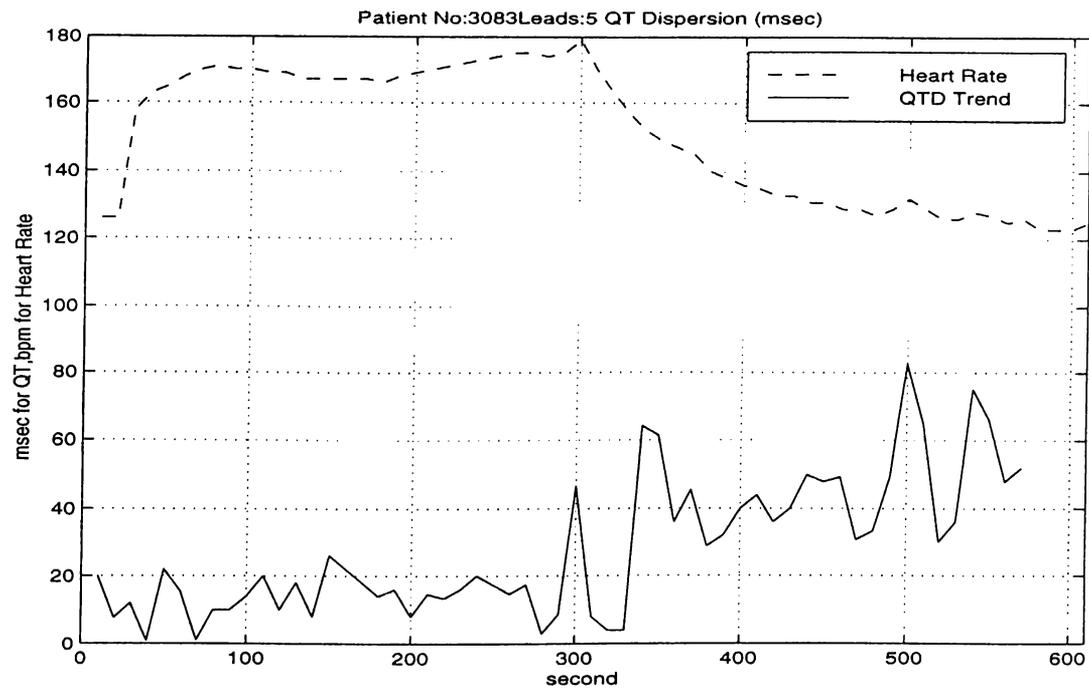


Figure A.65: QTD and Heart Rate for patient 3083 ST=+ QT=+ A=?

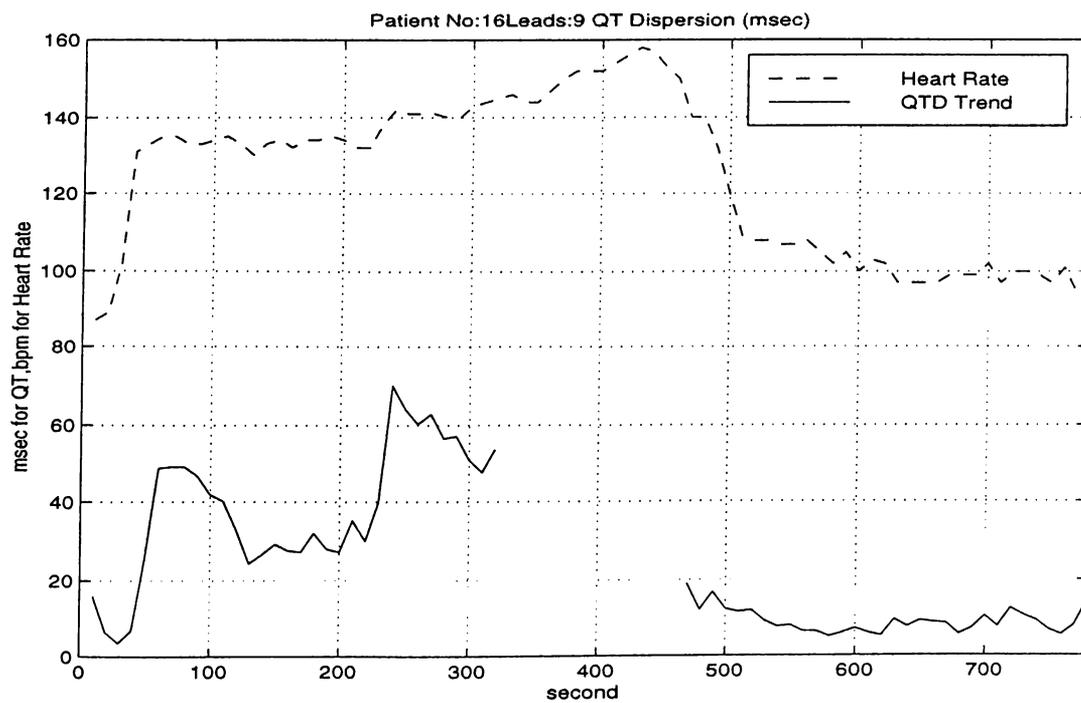


Figure A.66: QTD and Heart Rate for patient 16 ST=+ QT=+ A=?

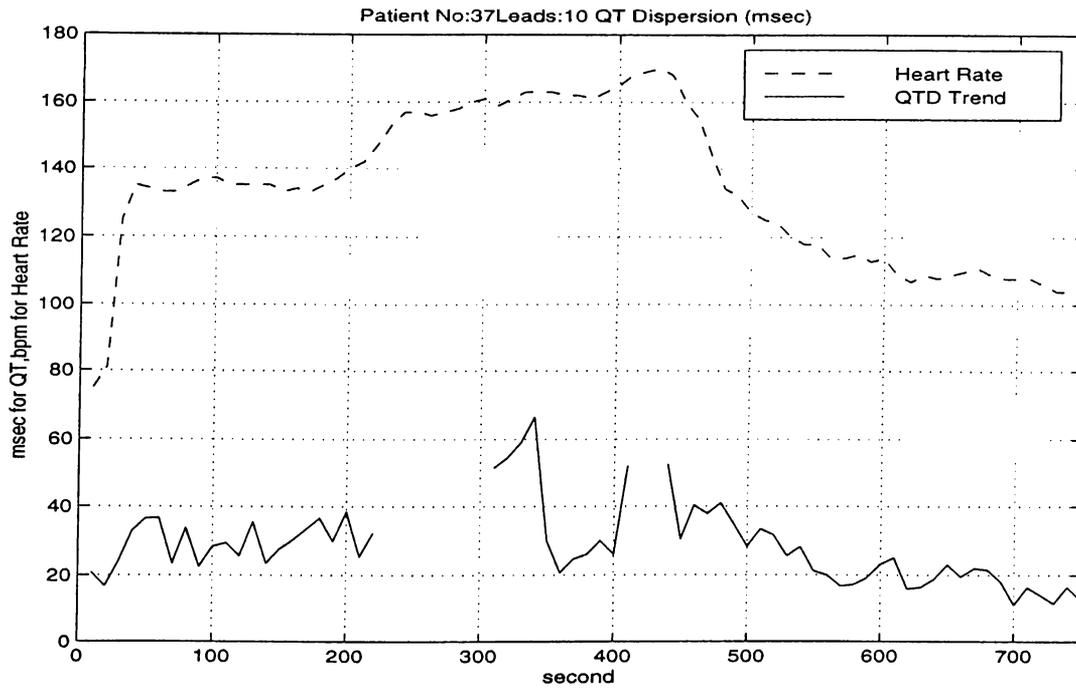


Figure A.67: QTD and Heart Rate for patient 37 ST=+ QT=+ A=?

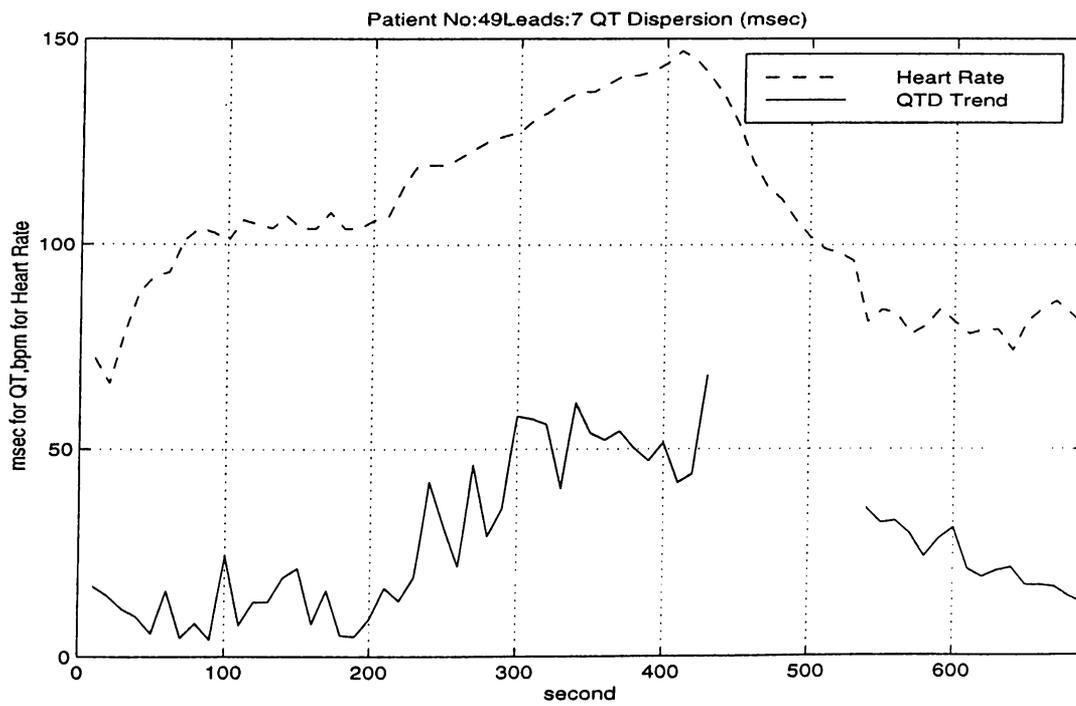


Figure A.68: QTD and Heart Rate for patient 49 ST=+ , EXT

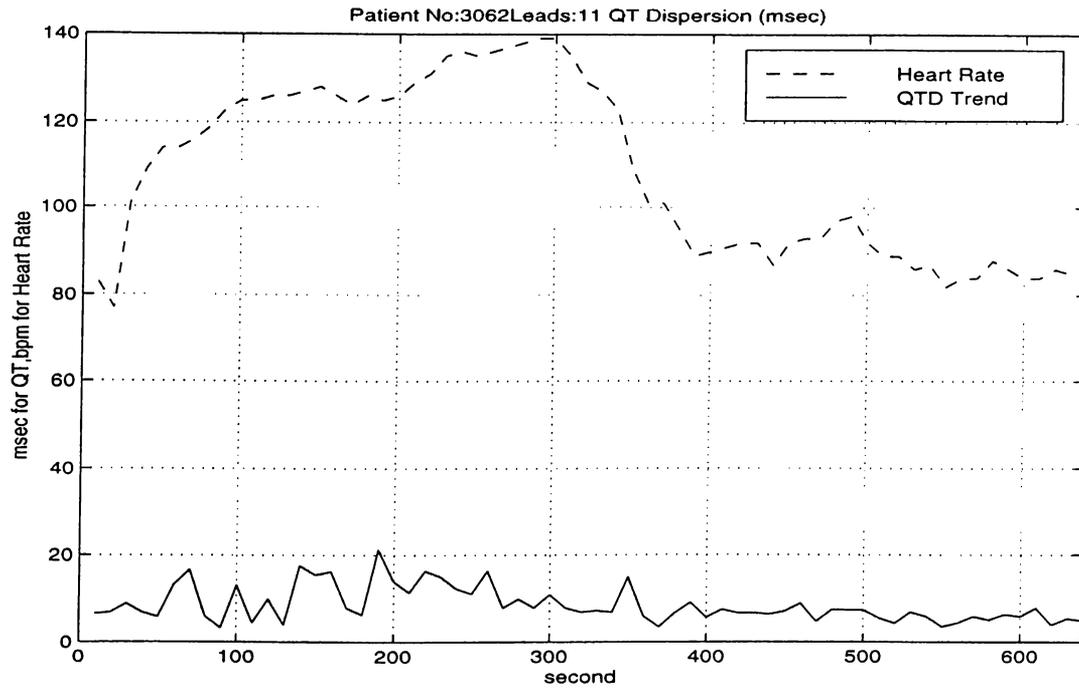


Figure A.69: QTD and Heart Rate for patient 3062 ST=+ , EXT

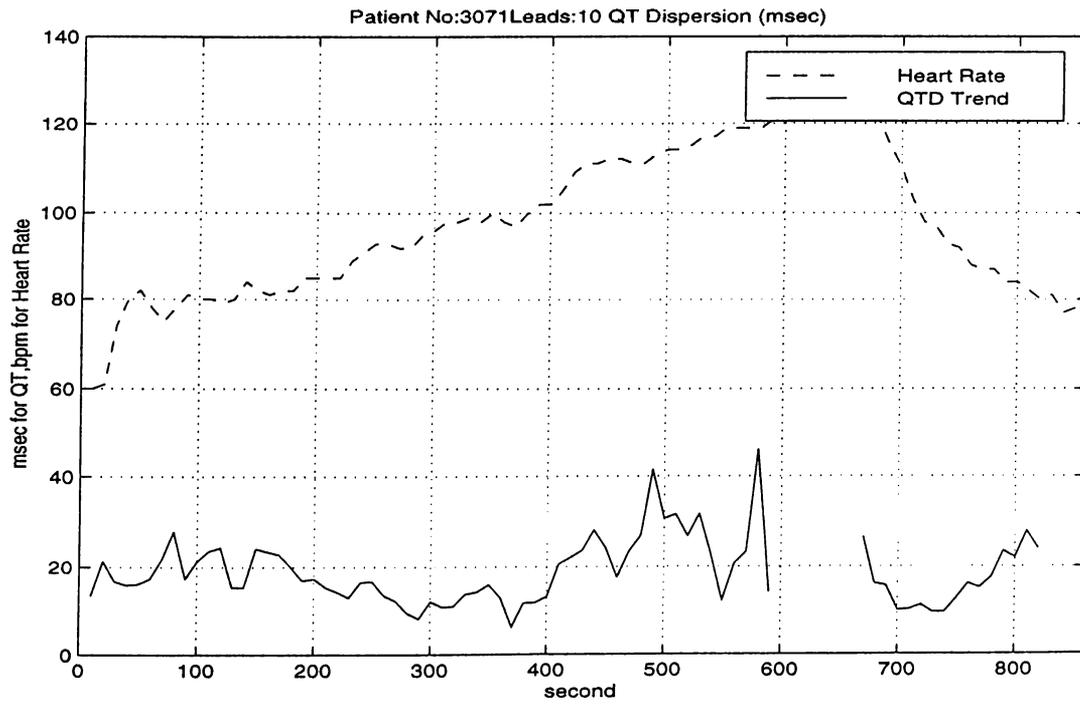


Figure A.70: QTD and Heart Rate for patient 3071 ST=+ , EXT

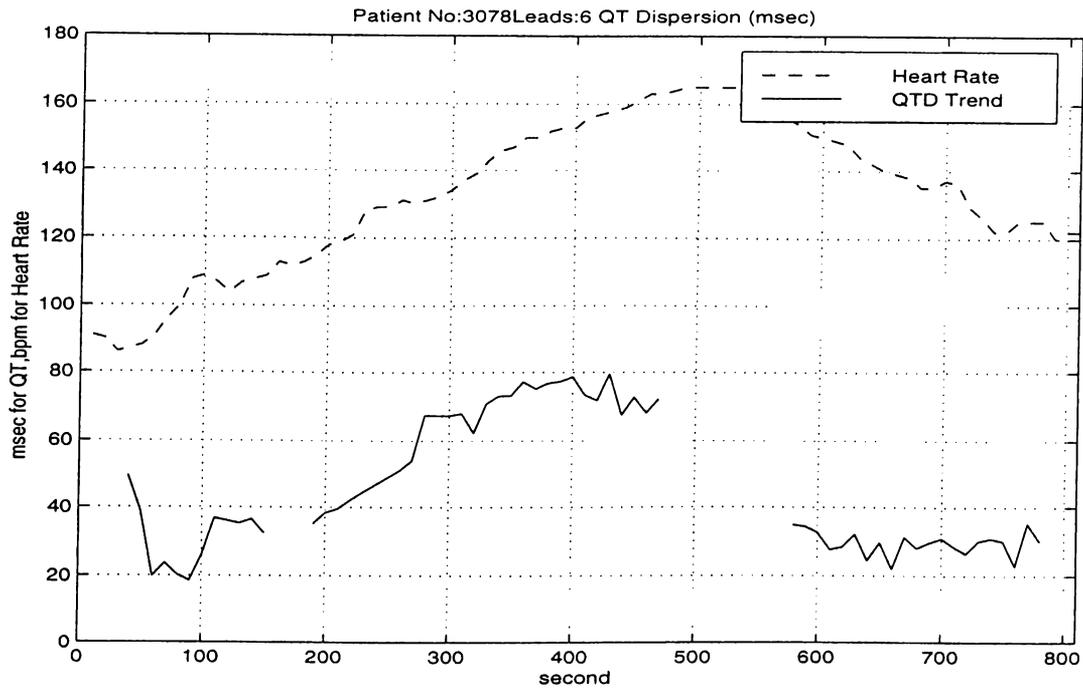


Figure A.71: QTD and Heart Rate for patient 3078 ST=+ , EXT

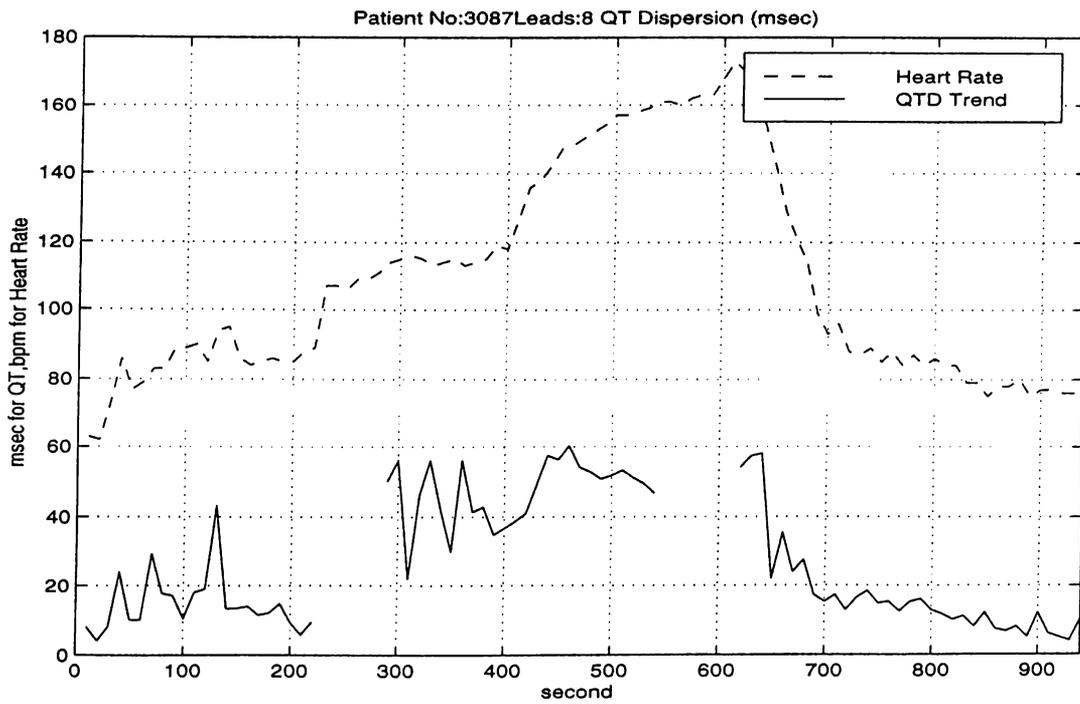


Figure A.72: QTD and Heart Rate for patient 3087 ST=+ , EXT

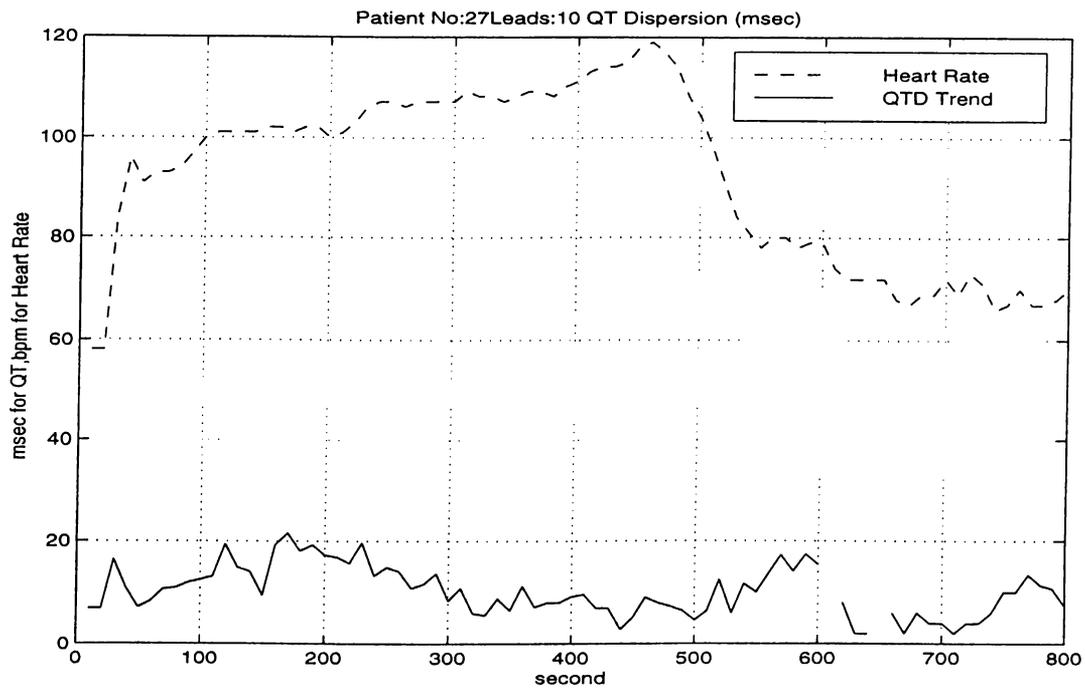


Figure A.73: QTD and Heart Rate for patient 27 ST=+ , EXT

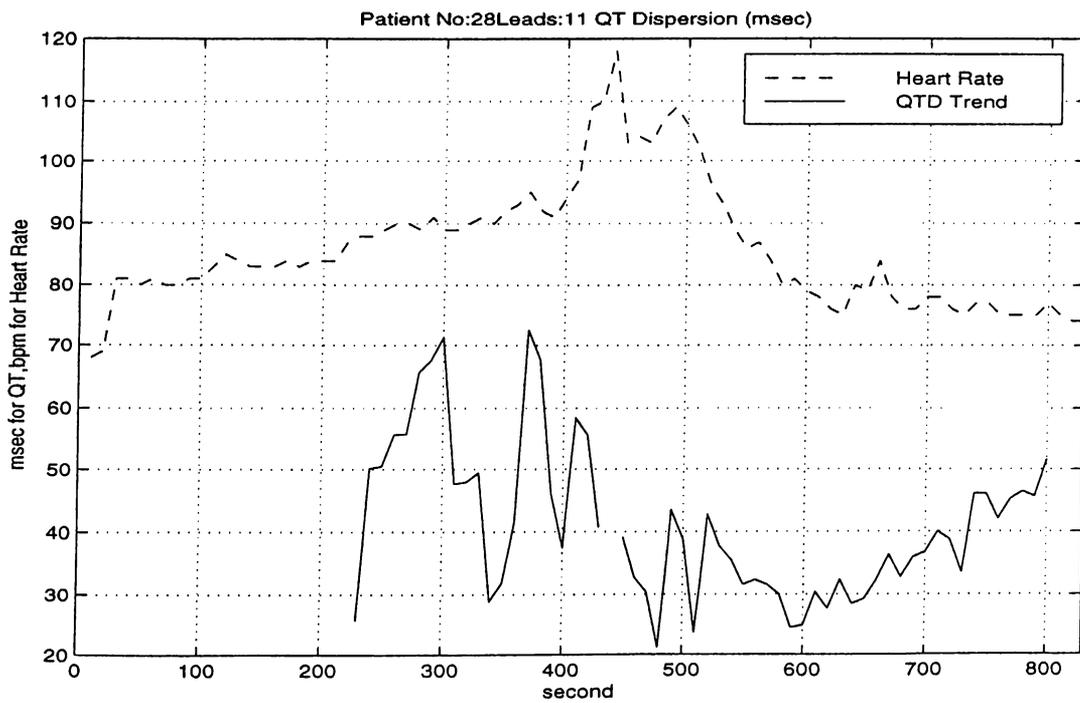


Figure A.74: QTD and Heart Rate for patient 28 ST=+ , EXT

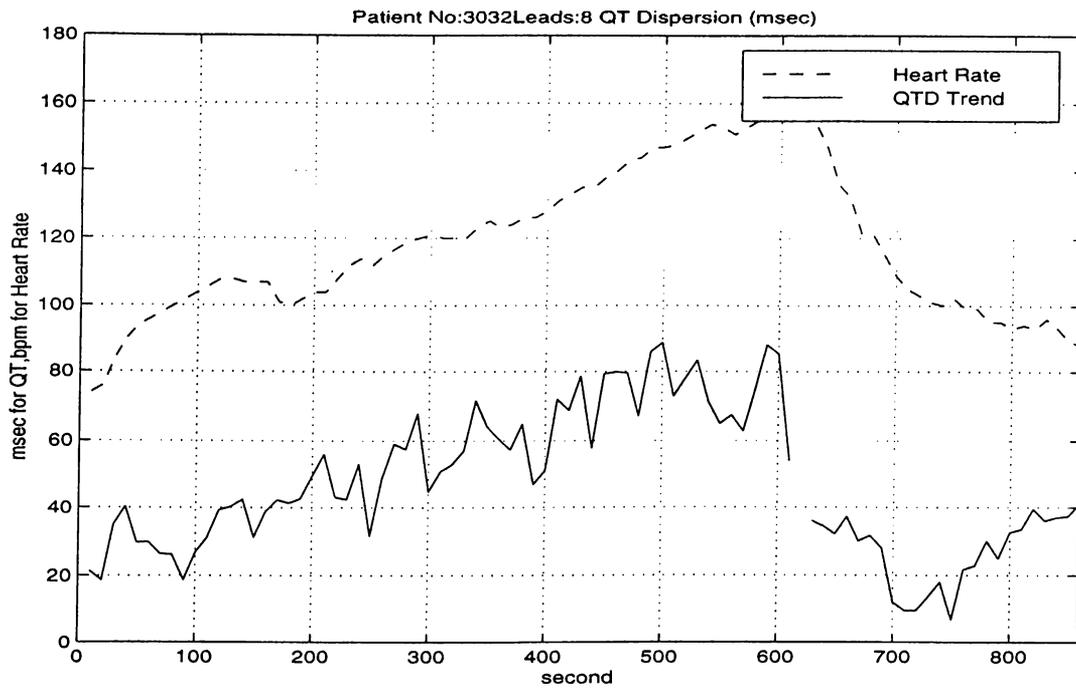


Figure A.75: QTD and Heart Rate for patient 3032 ST=- QT=+ A=?

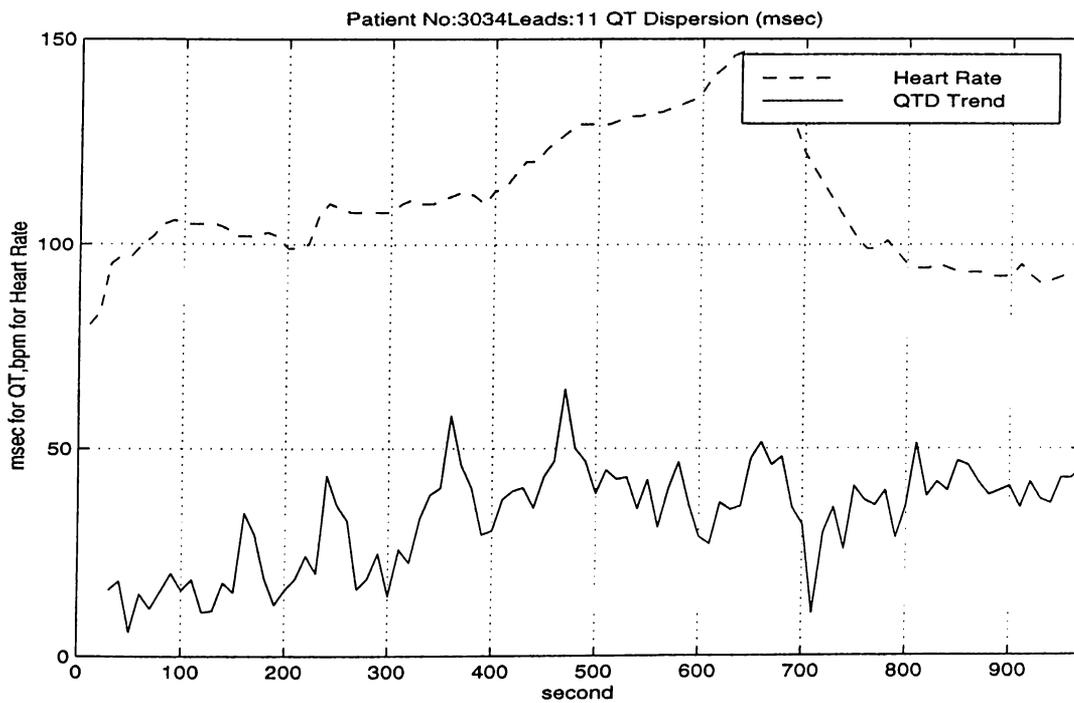


Figure A.76: QTD and Heart Rate for patient 3034 ST=- QT=+ A=?

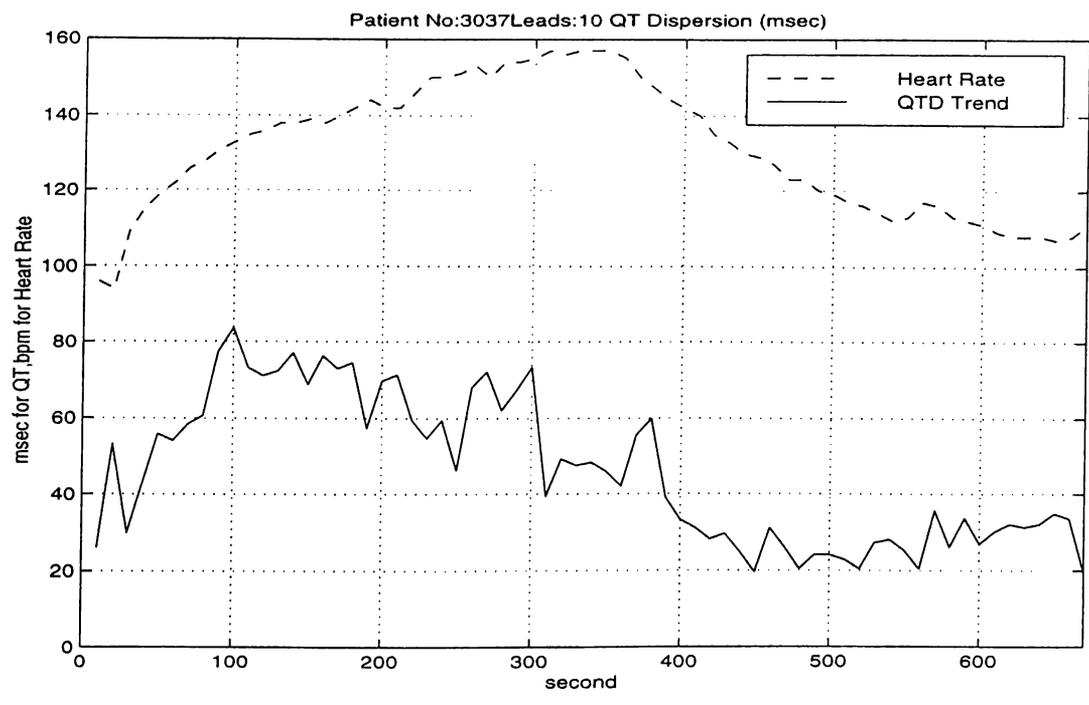


Figure A.77: QTD and Heart Rate for patient 3037 ST=- QT=+ A=?



Figure A.78: QTD and Heart Rate for patient 3077 ST=- QT=+ A=?

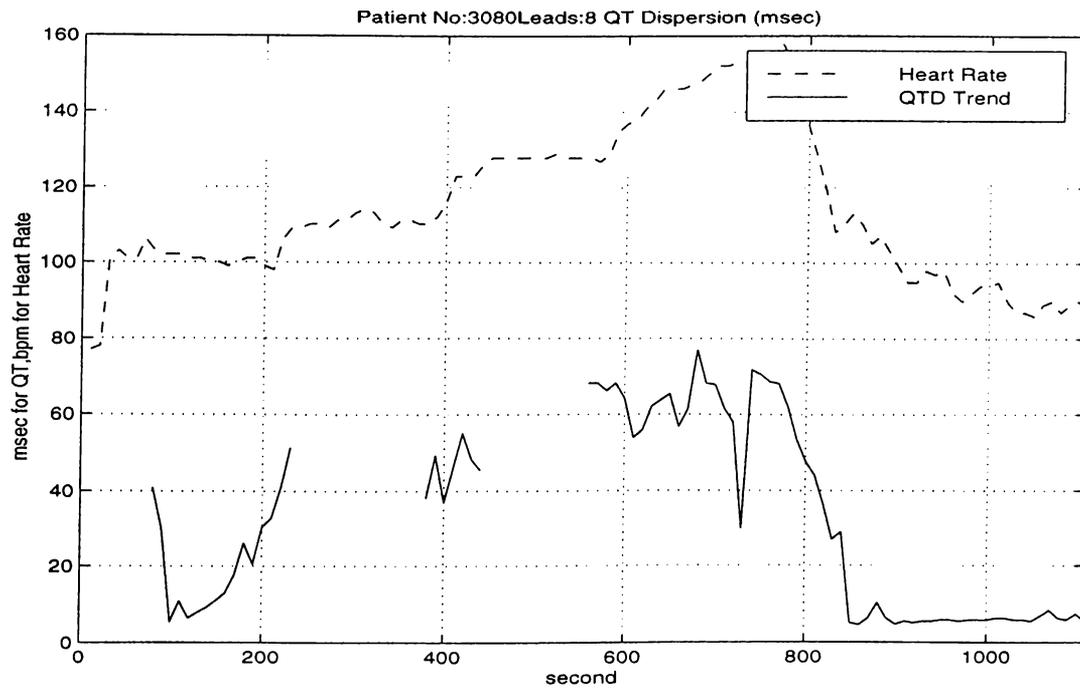


Figure A.79: QTD and Heart Rate for patient 3080 ST=- QT=+ A=?

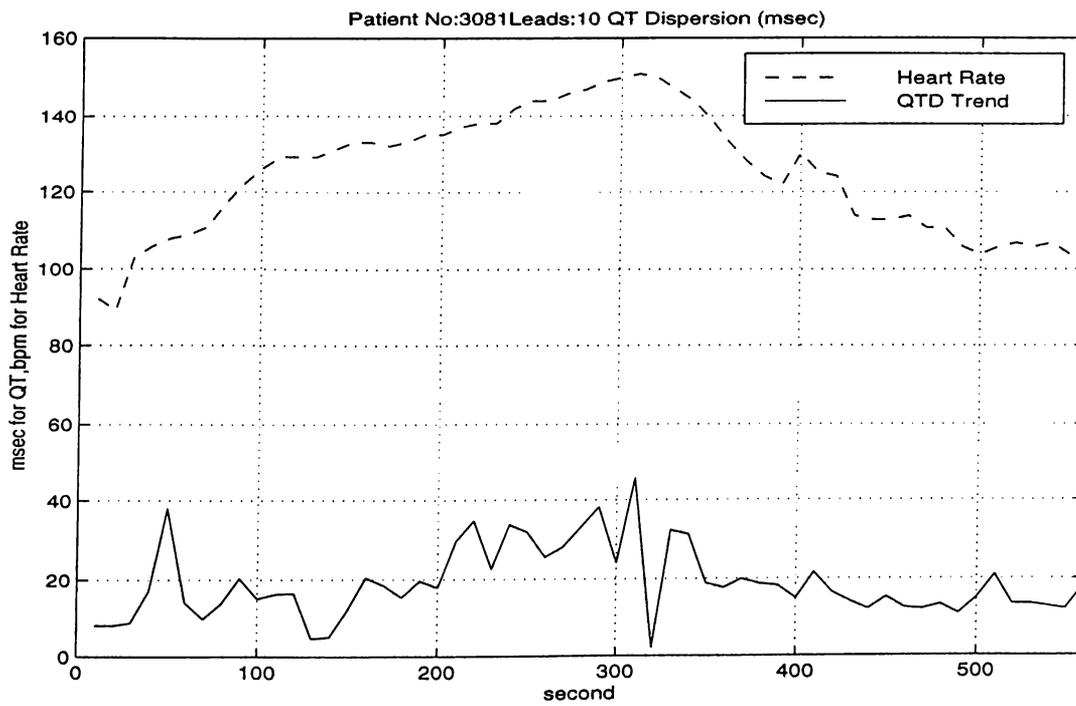


Figure A.80: QTD and Heart Rate for patient 3081 ST=- QT=+ A=?

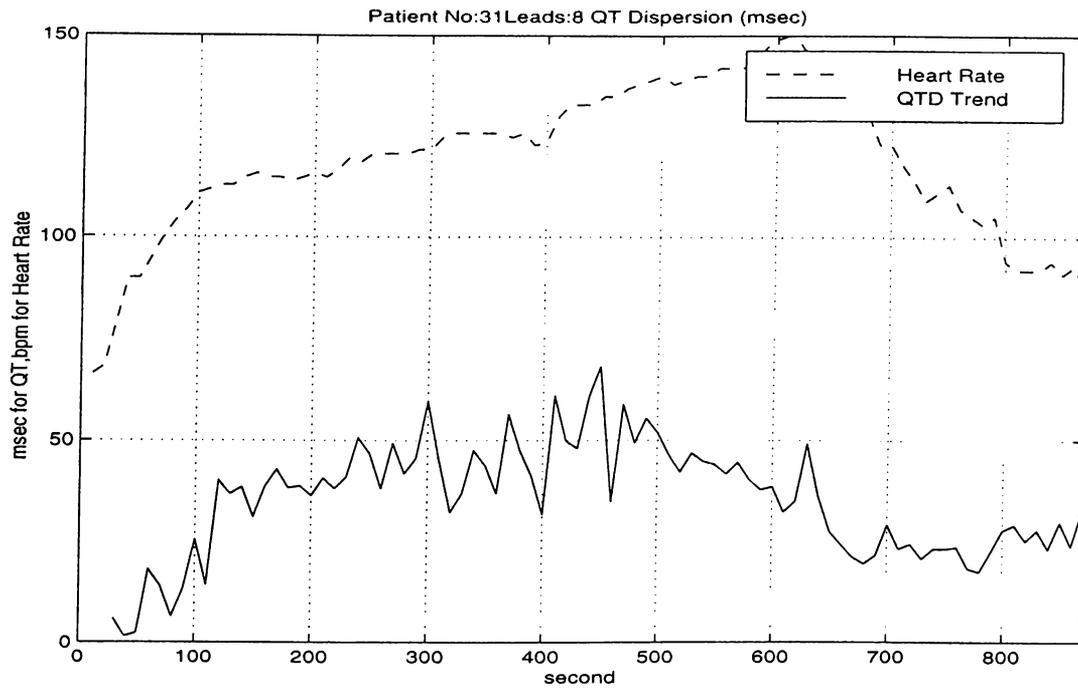


Figure A.81: QTD and Heart Rate for patient 31 ST=- QT=+ A=?

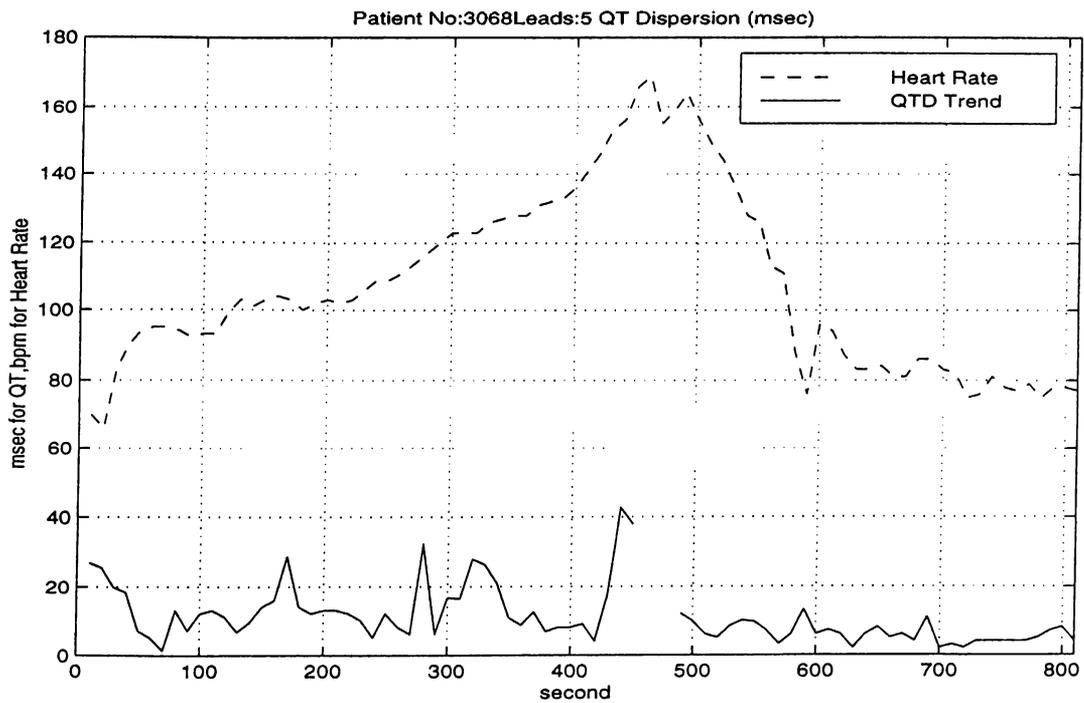


Figure A.82: QTD and Heart Rate for patient 3068 ST=+ QT=- A=-

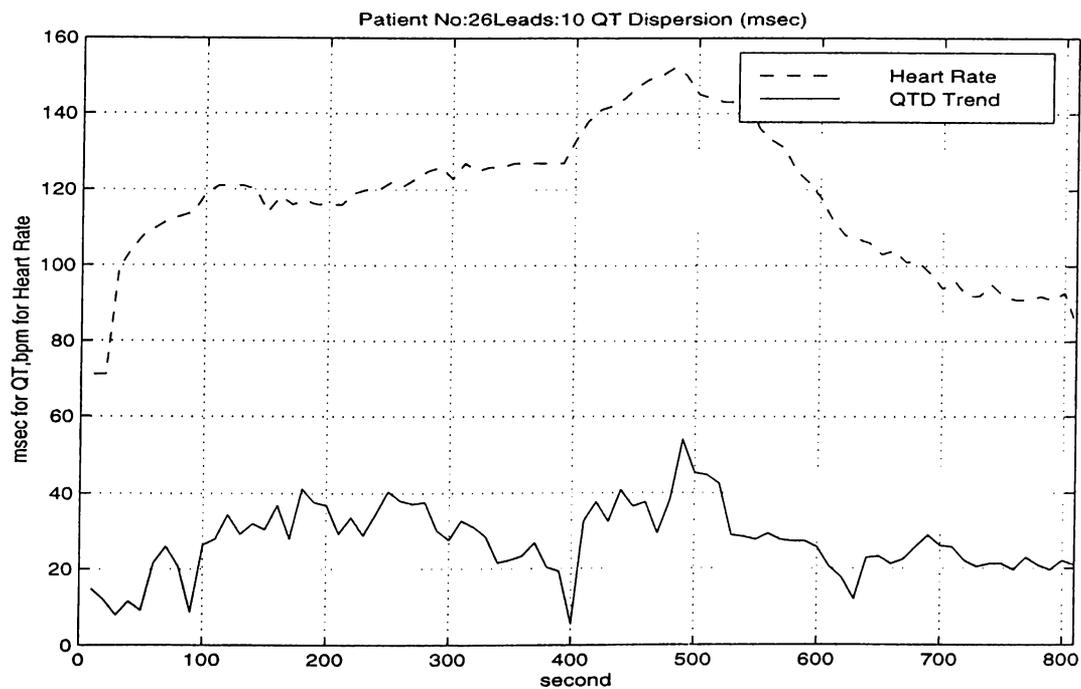


Figure A.83: QTD and Heart Rate for patient 26 ST=+ QT=- A=?

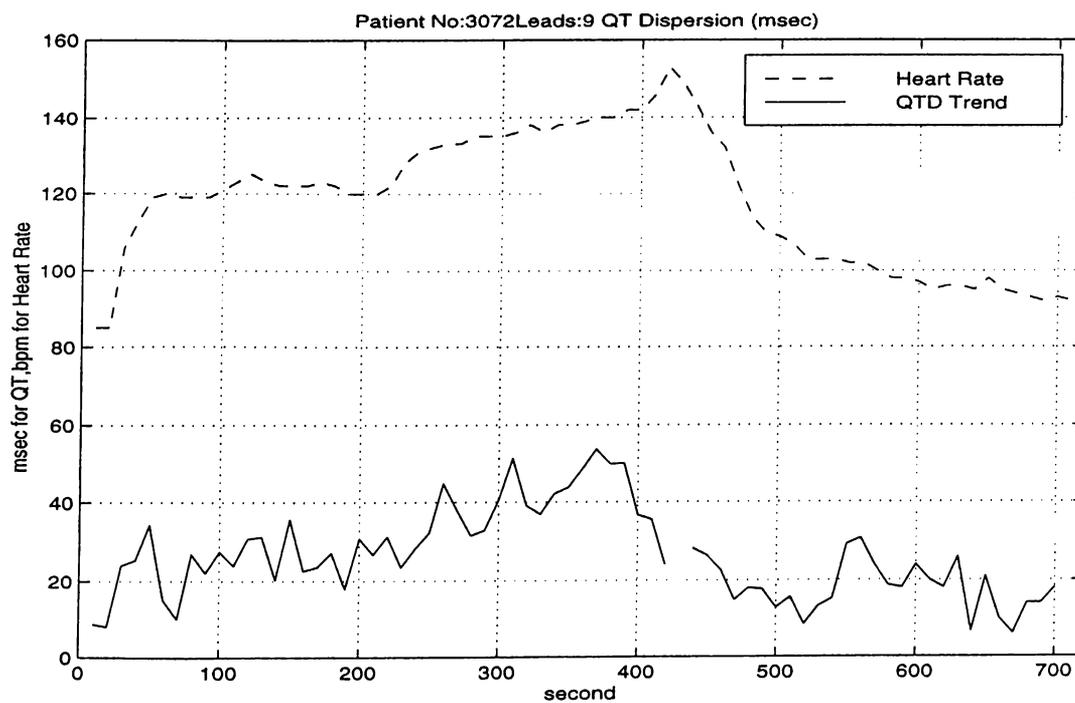


Figure A.84: QTD and Heart Rate for patient 3072 ST=+ QT=- A=?

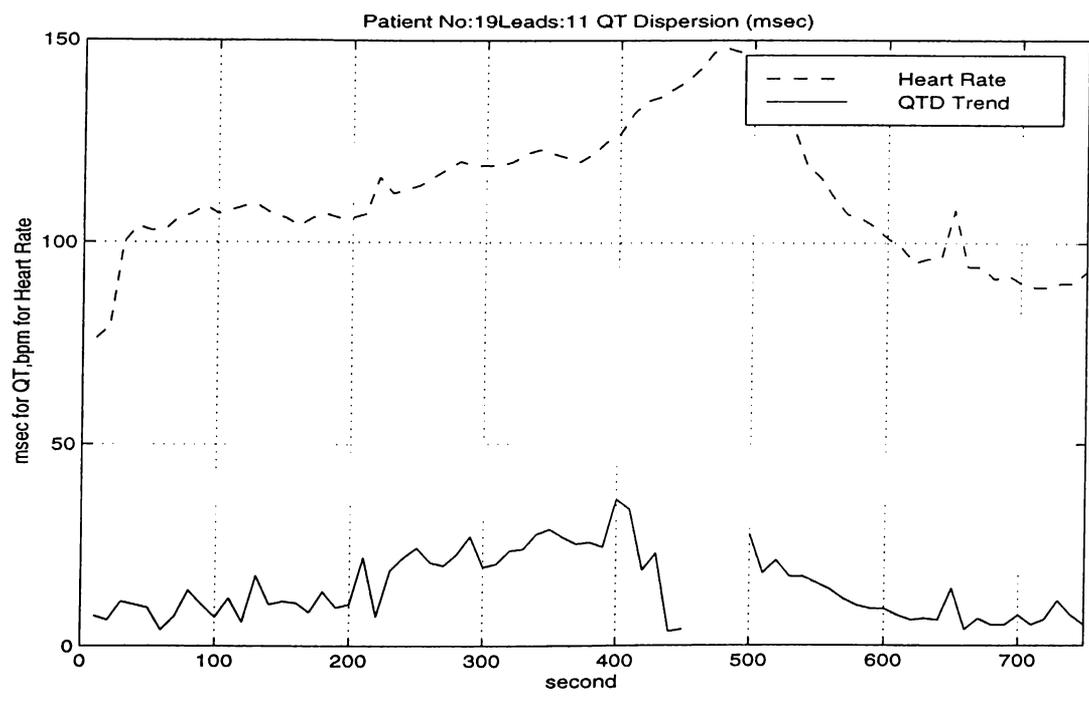


Figure A.85: QTD and Heart Rate for patient 19 ST=+ QT=- A=?

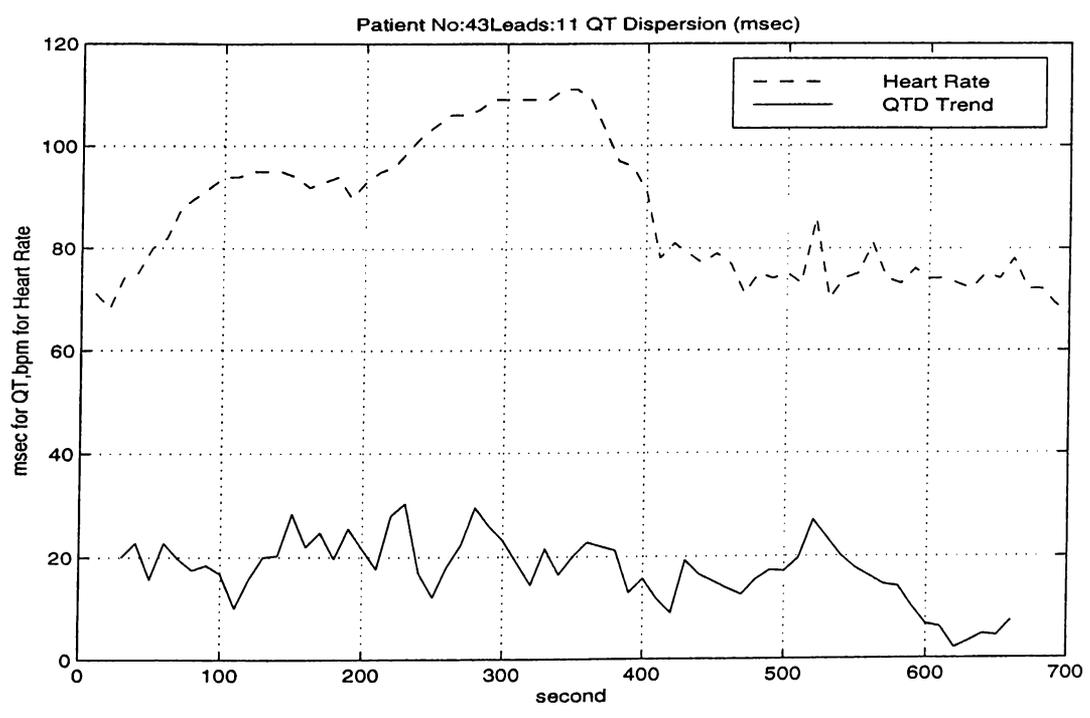


Figure A.86: QTD and Heart Rate for patient 43 ST=+ QT=- A=?

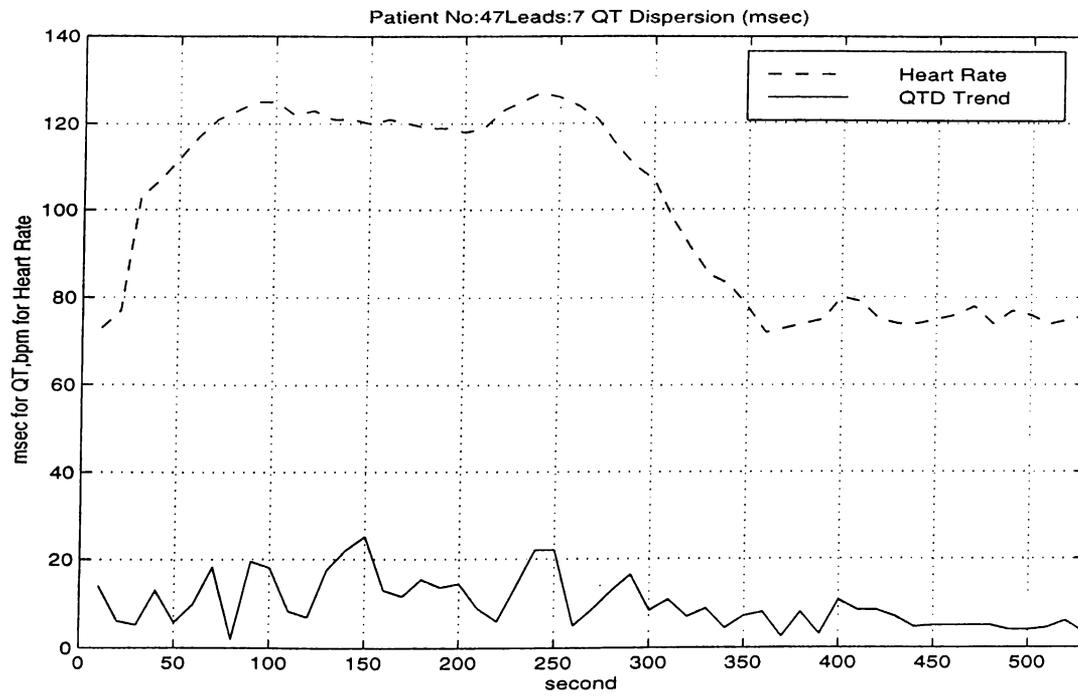


Figure A.87: QTD and Heart Rate for patient 47 ST=+ QT=- A=?

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