

# Relationship Between 12-Lead ECG QT Dispersion And 3D-ECG Repolarization Loop

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## Abstract

*Detection of QT dispersion on 12 Lead surface electrocardiogram has been proved to be a strong prognostic index of malignant events and it is thought to be closely related to an heterogeneity in the repolarization wavefront.*

*This work aims to correlate QT dispersion with the morphology of the spatial T wave loop. Indexes of planarity and geometry are derived from the 3D-ECG repolarization loop with a validated algorithm (CAVIAR). Multiple regression analysis indicates that QT dispersion measured on 12 standard lead is significantly correlated with a loss of planarity and with a wider shape of the loop.*

*QT dispersion is then closely related to a spatial distortion of the cardiac vector during the repolarization phase and can be indirectly evaluated on the 3D electrocardiogram.*

## 1. Introduction

Repolarization dispersion refers to an heterogeneity of the repolarization process, either due to a localized delay of activation or to a longer action potential duration of specific regions of the myocardium. This phenomenon has been observed within a wide variety of cardiac disorders and it has been shown to constitute a substrate for malignant arrhythmias [1]. Unfortunately, a direct and non invasive measure of repolarization heterogeneity is difficult to obtain (apart of mapping with more than 100 leads). However, since several years, repolarization dispersion is directly evaluated on the surface 12-lead ECG by means of the so-called QT dispersion (also referred to as interlead QT variability) which is defined as the difference in the QT interval as measured on a maximum of 12 ECG leads [2]. Despite the reduced number of exploring sites, the good prognosis of QT dispersion has been demonstrated in different pathologies [3]. Surprisingly, no attempt to discern the implication on the 3D electrocardiogram has been made until today.

The aim of this work is to investigate on 3D-ECG which morphological parameters of the spatial T-loop may be correlated with the 12-lead QT dispersion. This findings may indeed lead to a better understanding on the actual meaning of the phenomenon and facilitate its assessment. In addition, the direct evaluation of 3D-ECG loops obtained from orthogonal Holter leads could allow the inspection of repolarization dispersion under a dynamic perspective and help to discern the role played by the autonomic nervous system.

## 2. Methods

### 2.1 Scalar Measurements

The study population consisted of 37 subjects belonging to 3 specific subgroups: 14 normals (age:  $26 \pm 5$  years), 11 post-myocardial infarction patients (age:  $57 \pm 11$  years) and 12 subjects with Long QT syndrome (age:  $29 \pm 18$  years).

All subjects were recorded with a MAC15 electrocardiograph (Marquette Electronics Inc.). This device enables direct recording of 8 standard leads (6 precordial plus 2 limb leads) and of 3 additional leads, which in our case were the Frank XYZ orthogonal derivations. The remaining 4 standard leads are internally calculated. The 15 digitized recorded leads (250 Hz, 5  $\mu$ volt) were transferred to a PC for quantitative analysis where a dedicated semi-automatic algorithm performed the analysis of QRS-T complexes in each individual lead. The algorithm automatically detects the position of onset and offset of both the QRS complex and T waves by a methodology described in [4]. An user can subsequently validate the automatic measurements and eventually override them by manually changing the positions of the fiducial points. In particular, all the leads where the T wave offset could not be clearly confirmed (either for noise content or for aberrant shape) were discarded from the analysis. The 12-lead QT dispersion (QTd) was expressed as the standard deviation of the QT durations of the accepted leads.

## 2.2 The CAVIAR 3-D Algorithm

The 3D analysis was achieved with the employ of a well-known program (CAVIAR) which was directly applied to the digitized Frank XYZ derivations. A main feature of CAVIAR is to evaluate a 3D loop (in our case the T-wave loop) in the space defined by its 3 principal axes of inertia [5]. In this space, the shape of the loop is determined by the 3 eigenvalues relative to the principal axes:  $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$ . In general, the energy of the loop is concentrated in a plane (called the preferential plane) so that the value of  $\lambda_3$  is small with respect to the one of  $\lambda_1$  and  $\lambda_2$ . Furthermore, in the preferential plane, the T loop is usually narrow (ellipsoidal shape), thus leading to a value of  $\lambda_2$  smaller than the value of  $\lambda_1$ .

The morphological distortion of the T-loop was analyzed by defining a parameter of planarity PL and a parameter of planar geometry (or shape in the preferential plane) PG as follows:

$$PL = 100 - \frac{100 \lambda_3}{\lambda_1 + \lambda_2 + \lambda_3} \quad PG = \frac{\lambda_2}{\lambda_1}$$

PL evaluates the importance (expressed in percent value) of the smallest eigenvalue with respect to the first two. For a globally planar loop,  $\lambda_3$  is 0 and PL becomes 100. PG is an indicator of the loop-shape in the preferential plane; a narrow loop will have a smaller value of PG whereas a circular loop will have PG approaching 1.

## 2.3 Statistical Analysis

Differences of mean values of QTd, PL and PG were compared between the two pathological populations and the normal population with Student's t-test.

The correlation between the morphological parameters and QTd was investigated with both univariate and multivariate stepwise regression analyses. In the multivariate approach, the multiplication term PL\*PG was also added to the model to take into account the interactions between the two morphological parameters.

## 3. Results

Table 1 summarizes the t-test results: QTd was significantly larger in the two pathological populations whereas for the morphological parameters only PG in post infarction provided a significant increase. Changes in PL were numerically very small; even in the most extreme case (a Long QT patient with apparent loss of planarity), the value of PL was 98.1, thus indicating that the vast majority of the T wave loop is essentially always contained in a plane.

Both PL and PG were significantly correlated to QT dispersion ( $-0.48$   $p=0.003$ ,  $0.53$   $p=0.001$  respectively). With the multiple regression analysis applied to both

parameters as well as to their interaction, the correlation obtained was  $0.68$  ( $p < 0.001$ ); Table 2 shows the results relative to the multiple regression analysis. The interaction term and PG were selected by the model whereas PL alone was not significant. The negative sign of the interaction term is due to PL, as it was for the univariate analysis. Figure 1 depicts the output of the multiple regression model versus the scalar QT dispersion. Figure 2 shows the spatial T loop and the projections on the planes of inertia for a case with small dispersion (QTd = 9.5 msec) and for a case with a large one (QTd = 26.8 msec). The distortion, and in particular the loss of planarity, are noteworthy. Figure 3 depicts the overlapped recorded leads of a subject with evident QT dispersion.

	Norm	Post MI	Long QT
QTd	8.5±2.6	24±9.7*	22.2±13.8 *
PL	99.91±0.22	99.84±0.14	99.5±0.55
PG	0.078±0.09	0.247±0.21*	0.16±0.18

Table 1: Means±stand. dev. of study variables in the three populations; \* denotes a significant t-test when compared to the normal group.

	Coeff	ST DEV	P
PG	550.8	246.3	0.032
PL*PG	-53.58	25.27	0.042

Table 2: Results of multiple Regression Analysis.

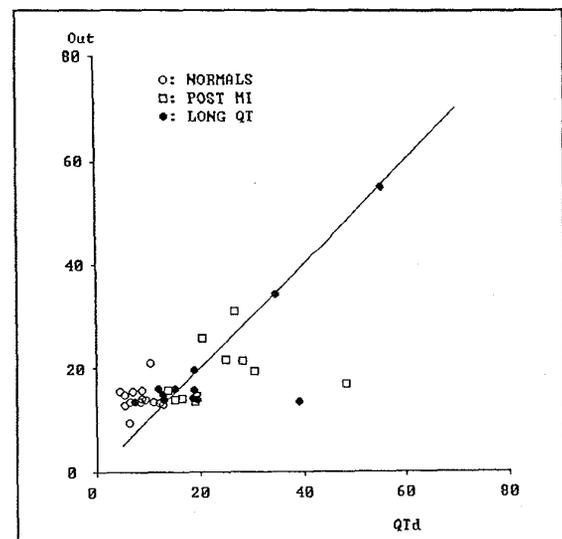


Figure 1: Scatterplot of output of multiple regression model vs QTd.

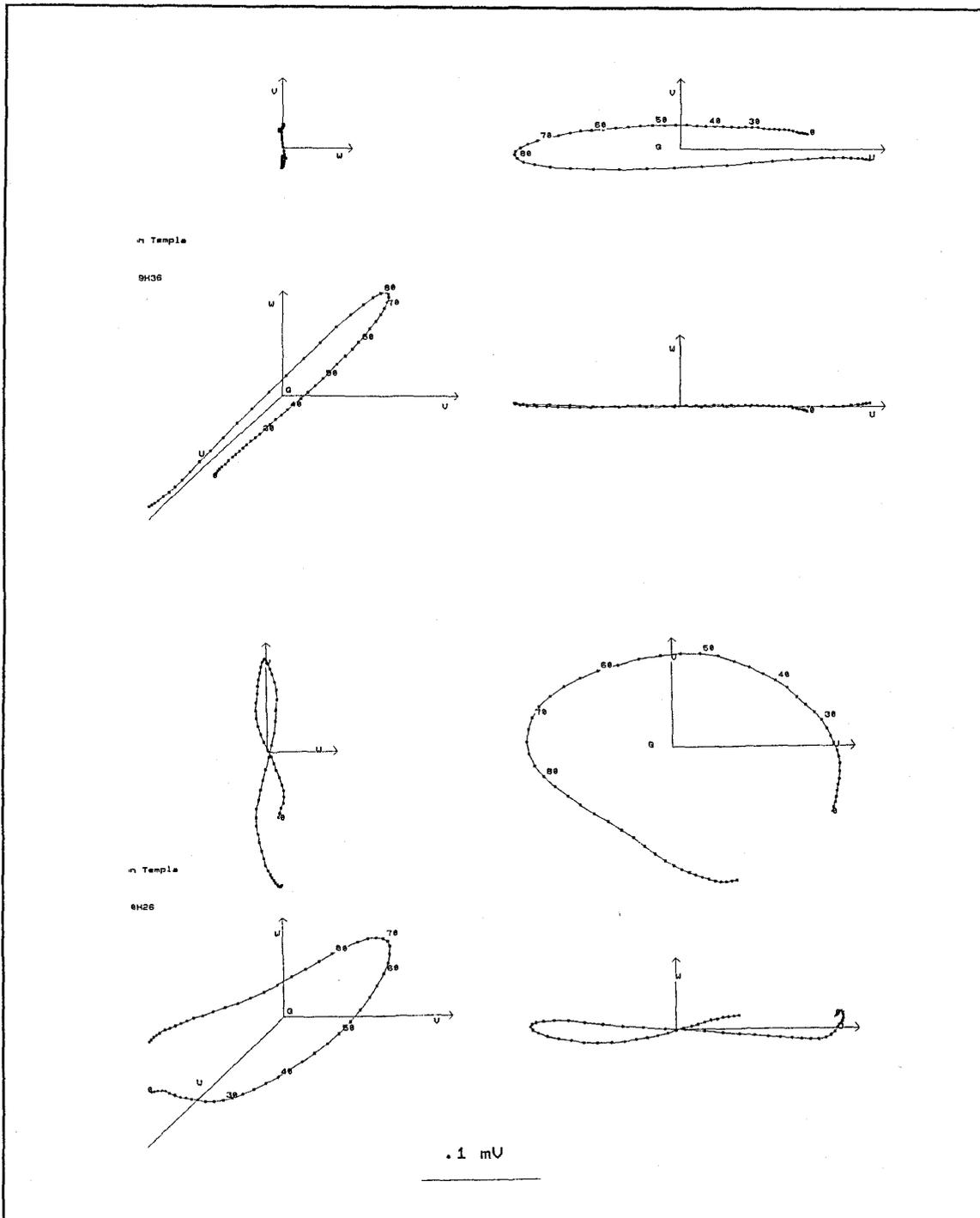


Figure 2: Examples of T wave loops in two representative cases: the top panel is relative to a normal subject ( $QTd = 9.5$  msec,  $PL = 99.9$ ,  $PG = 0.03$ ) and the bottom panel is relative to a post infarction patient ( $QTd = 26.8$  msec,  $PL = 99.61$ ,  $PG = 0.55$ ). For each panel the 3D loop is visualized in the lower left part and the three projections on the inertia planes in the adjacent zones (the projection in the preferential plane is the upper right one). Despite a numerically small decrease of PL, the change in the planarity (visible in upper left and lower right projections of each panel) is evident. Note also the almost circular shape of the second loop (upper right projection).

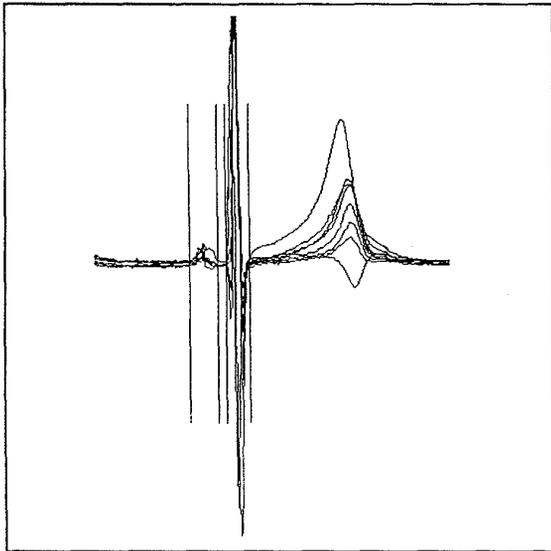


Figure 3: Overlapping of 8 measured leads for a subject with evident QT dispersion; The beats are aligned with respect to the QRS onset.

#### 4. Discussion

This study provides evidence that interlead QT variability is associated with morphological changes in the 3D-loop of the T wave. In particular, loss of planarity and wider (less ellipsoidal) geometry are significantly correlated with increased QT dispersion.

This findings lead to two direct consequences: on one side we obtained further confirmation that QT dispersion measured on 12 lead ECG is indeed the result of an altered repolarization process and not simply an artifact due to lead configuration. This is in concordance with what has been recently observed by correlating repolarization dispersion assessed by 12-lead ECG and directly recorded monophasic action potential [6].

The second important consequence of this work is that we can conclude that the information of QT dispersion is contained in the spatial T loop. This opens up the issue of whether a vectorcardiography methodology may be suitable. The 3D approach is certainly preferable as it avoids the scalar lead projection effects and, most importantly, it minimizes several technical flaws that are known to affect the evaluation of QT dispersion on the surface ECG [2][7]. Above all, the problem of correctly determining the offset of the T wave. Indeed, scalar approaches imply the determination of each lead T wave offset, for which an accepted and reliable method has not yet been found.

At the moment, whether vectorcardiography should provide a better prognosis index than conventional 12 lead ECG in pathological populations remains questionable. As a matter of fact, as it has been shown in the field of diagnostic quantitative ECG [8], the best performance

may be obtained from the combined use of scalar and 3D ECG (each method utilizing information neglected by the other one).

A limitation of this work is that the study population is still too small to allow more conclusive results. In particular, cases with larger QTd should be added (and the correlation should increase).

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