

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800

Open access books available

122,000

International authors and editors

135M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Quantification of Ventricular Repolarization Dispersion Using Digital Processing of the Surface ECG

Ana Cecilia Vinzio Maggio<sup>1</sup>, María Paula Bonomini<sup>2</sup>,  
Eric Laciár Leber<sup>3</sup> and Pedro David Arini<sup>1,2</sup>

<sup>1</sup>*Instituto Argentino de Matemática 'A. Calderón', CONICET, Buenos Aires*

<sup>2</sup>*Instituto de Ingeniería Biomédica, Universidad de Buenos Aires, Buenos Aires*

<sup>3</sup>*Gabinete de Tecnología Médica, Universidad Nacional de San Juan, San Juan  
Argentina*

## 1. Introduction

Digital processing of electrocardiographic records was one of the first applications of signal processing on medicine (Taback et al., 1959). There are many ways to analyze and study electrical cardiac activity using the surface electrocardiogram (ECG) and nowadays a good clinical diagnostic and prevention of cardiac risk are the principal goal to be achieved (Sörnmo & Laguna, 2005).

One aim of digital processing of ECG signals has been quantification of ventricular repolarization dispersion (VRD), phenomenon which is mainly determined by heterogeneity of action potential durations (APD) in different myocardial regions (Amlie, 2000). The APD differs not only between myocytes of apex and the base of both ventricles, but those of endocardial and epicardial surfaces (transmural dispersion) and between both ventricles. Also, it was demonstrated the existence of several electrophysiologically and functionally different myocardial cells, like epicardial, endocardial and mid-myocardial M cells (Antzelevitch et al., 1999). The APD inequalities develop global and/or local voltage gradients that play an important role in the inscription of ECG T-wave morphology. In this way, we can assume that T-wave is a direct expression of ventricular repolarization (VR) inhomogeneities on surface ECG.

Experimental and clinical studies have demonstrated a relationship between VRD and severe ventricular arrhythmias (Kuo et al., 1983) (Surawicz, 1997). In addition, patients having increased VRD values have a higher risk of developing reentrant arrhythmias (Shimizu & Antzelevitch, 1998). Frequently the cardiac answer to several pathological states produces an increase of VRD; this phenomenon may develop into malignant ventricular arrhythmia (MVA) and/or sudden cardiac death (SCD). Moreover, it has been shown that the underlying mechanisms in MVA and/or SCD are cardiac re-entry, increased automation, influence of autonomic nervous system and arrhythmogenic substrates linked with cardiac pathologies. These cardiac alterations could be present in ischemia (Janse et al., 1985), hypothermia (Eagle, 1994), electrolyte imbalance (Weinberg et al., 1995), long QT syndrome (LQTS) (Priori et al., 1994), autonomic system effects (Shusterman et al., 1998) and others.

Digital processing of ECG has been proved to be useful for cardiac risk assessment, with additional advantages like its non invasive nature and direct applicability to the general population (Sörnmo & Laguna, 2005). Also, with the aim to identify high cardiac risk patients, the researchers have tried to quantify the VRD with different parameters obtained from mathematic-computational processing of the surface ECG. These parameters are based on detecting changes of T-wave intervals and T-wave morphology during cardiac pathologies, linking these changes with VRD.

Figure 1 illustrates a temporal segment of an ECG acquired in a healthy subject, which includes the representation of different waves, intervals and segments of the cardiac signal. The P-wave reflects the sequential depolarization of the right and left atria, the QRS complex (consisting of Q, R and S waves) reveals the depolarization of both ventricles, and the T-wave displays the VR. The RR interval represents the duration of a cardiac cycle. The QT interval corresponds to the time from the onset of ventricular depolarization to the offset of VR.

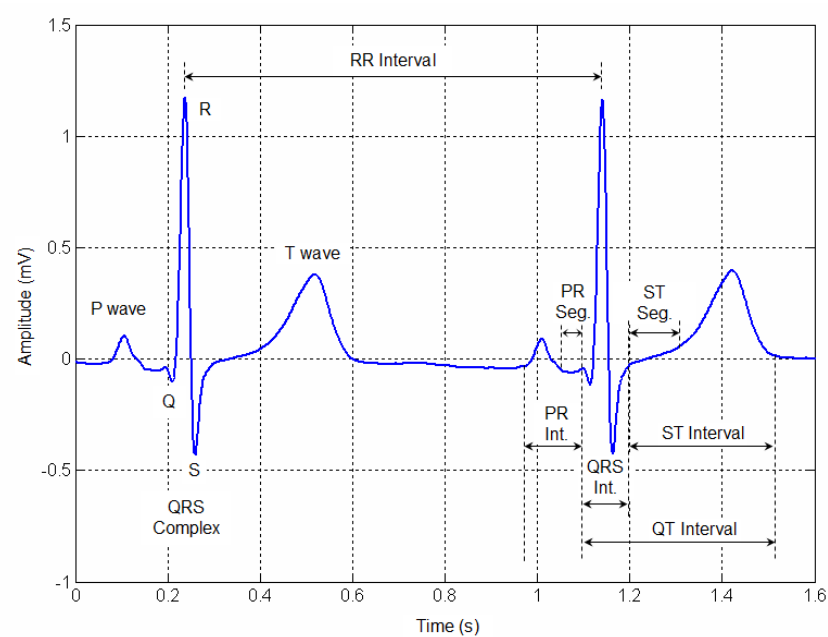


Fig. 1. Schematic representation of ECG waves, intervals and segments for a healthy subject.

In this chapter, we present a review of VRD indexes based on digital processing of ECG signals to quantify cardiac risk. The chapter is organized as follows: Section 2 explains ECG preprocessing and delineation of fiducial points. In Section 3, indexes of VRD quantification, such as: QT interval dispersion, QT interval variability and T-wave duration, are described. In Section 4, different repolarization indexes related to T-wave morphology and energy are examined, including complexity of repolarization, T-wave residuum, angle between the depolarization and repolarization dominant vectors, T-wave morphology dispersion, micro T-wave alternans, T-wave area and amplitude and T-wave spectral variability. Finally, in Section 5 conclusions are presented.

1.1 Most used abbreviations

APD (action potential duration),  $C_D$  (Dipolar Components),  $C_{ND}$  (non-dipolar components),  $C_R$  (complexity of repolarization), DWT (dyadic wavelet transform), ECG (electrocardiogram), EMG (electromyogram), HR (heart rate), HRV (heart rate variability), HS (healthy subject), IL

(isoelectric line) **MAPs** (monophasic action potentials), **PVS** (premature ventricular stimulation), **QT<sub>C</sub>** (QT interval corrected), **QT<sub>D</sub>** (QT interval dispersion), **QT<sub>V</sub>** (QT interval variability), **SCD** (sudden cardiac death), **SVD** (singular value decomposition), **T<sub>CRT</sub>** (total cosine R-to-T), **T<sub>L</sub>** (T-wave loop), **T<sub>MD</sub>** (T-wave morphology dispersion), **T<sub>PE</sub>** (T-wave peak-to-end), **T<sub>W</sub>** (T-wave width), **T<sub>WR</sub>** (T-wave residuum), **T<sub>WRa</sub>** (absolute T-wave residuum), **T<sub>WRr</sub>** (relative T-wave residuum), **T<sub>WSV</sub>** (T-wave spectral variance), **μT<sub>WA</sub>** (micro T-wave alternans), **VF** (ventricular fibrillation), **VR** (ventricular repolarization) and **VRD** (ventricular repolarization dispersion).

## 2. ECG preprocessing

The objectives of ECG preprocessing consist on the application of several digital signal processing techniques in order to: a) attenuate the noise components present in the ECG signal, b) detect all heartbeats in the recording and, c) identify characteristics points of the ECG waves. In order to accomplish these objectives the following signal processing algorithms are used: ECG filtering, QRS complex detection and ECG delineation.

### 2.1 ECG filtering

Unfortunately, all ECG recordings are contaminated by different types of noise and artifacts sources (Sörnmo & Laguna, 2006) as it is illustrated in Figure 2. These noise sources are:

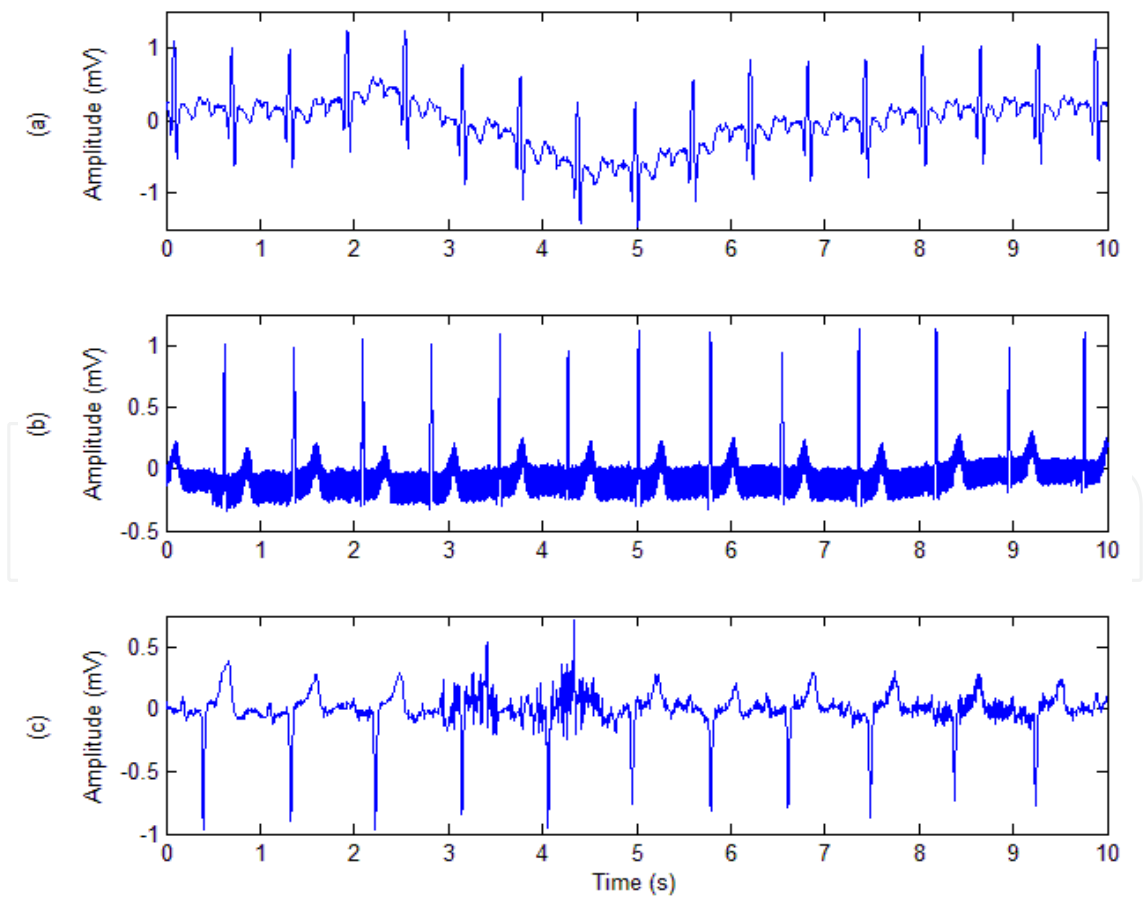


Fig. 2. Common types of noise in ECG recordings. (a) Baseline wander, (b) 50 Hz power line interference, and (c) Electromyographic noise.

a) *Baseline wander* is a low-frequency component in the ECG (see Fig. 2.a) caused by a variety of noise sources including respiration, body movements, and poor electrode contact. Its spectral content is usually confined to frequencies below 0.5 Hz. The magnitude of the baseline wander may exceed the amplitude of QRS complex by several times and it can significantly affect ECG analysis algorithms.

Different filtering techniques are employed for the removal of this low frequency noise, mainly, linear filters and polynomial fitting (Sörnmo & Laguna, 2005). In the first category, linear, time-invariant, highpass filters are used. The cut-off frequency ( $f_c$ ) and phase response characteristic should be chosen to preserve the morphology of ECG signal. The value of  $f_c$  must be lower than the minimum frequency of the ECG; a choice of  $f_c = 0.5$  Hz provides generally good results. A linear filter with time-variable cut-off frequency has been proposed for these ECG acquired during stress test (Sörnmo, 1993). Also, linear phase filters are recommended to prevent phase distortions in the ECG signal and avoid possible errors in the estimation of the wave durations and cardiac intervals. The second approach is to fit a polynomial to representative samples ("knots") of the ECG followed by the subtraction of the resultant polynomial curve. One knot must be defined for each beat, usually in the isoelectric line (IL) of PQ interval. In contrast to linear filtering, this approach requires that QRS complexes first be detected and PQ intervals are determined. After knots are located in the ECG signal, a third-order polynomial is fitted to these points (Sörnmo & Laguna, 2005).

b) *Powerline interference* is a common noise source in ECG recordings caused by electromagnetic fields of devices coupled to electric power system. It is characterized by a 50 or 60 Hz sinusoidal interference (see Fig. 2.b), which can be accompanied by its harmonics. Such narrowband noise makes difficult the further analysis of ECG record, and may affect the performance of the ECG delineation algorithms (Huhta & Webster, 1973). Various precautions may be taken during the acquisition of the ECG recording in order to minimize the level of the interference, such as shielding the leads, grounding property of the ECG system and lowering the skin-electrode impedance (Webster, 1992).

However, it may be still necessary to apply some signal processing to remove the residual powerline interference on the ECG recordings. For this purpose, simple techniques can be used such as straightforward linear bandstop or nonlinear filtering (Sörnmo & Laguna, 2005). A more advanced technique includes the amplitude and phase estimation of the interfering sinusoid in an isoelectric segment, followed by subtraction of the estimated sinusoid within the entire heartbeat (Ider & Köymnen, 1995). This last technique requires a correct delineation of PQ interval.

c) *Electromyographic noise* is due to the electrical activity of skeletal muscles during periods of contraction. It is particularly important in ECGs recorders during ambulatory monitoring or stress tests. It can be either intermittent, e.g. due to a sudden body movement (see Fig. 2.c), or have more stationary noise properties, e.g. during relaxation or sleep. The frequency components of electromyogram (EMG) noise considerably overlap those of the QRS complexes, making difficult their detection (Sörnmo & Laguna, 2005).

Due to the overlap spectra of both signals, EMG noise filtering is a complicated task which in several cases introduces considerable distortion in the ECG. Since the ECG is a repetitive signal, ensemble averaging is a commonly technique used for EMG noise reduction. However this technique is restricted to signal-averaged ECG analysis and can require much beats to be averaged particularly in ECG records corrupted with high levels of EMG noise (Laciar & Jané, 2001). Other different approach consists on the use of adaptive Gaussian filtering. This technique produces a time-varying lowpass filter with a variable frequency



response so that smooth segments on the ECG are subjected to considerable lowpass filtering whereas the QRS interval remains unfiltered (Talmon et al., 1986). The adaptation of the  $f_c$  of a linear lowpass filter with the slopes of the ECG has been proposed by Pinto (Pinto, 1991). Although others techniques have been proposed for EMG noise reduction, no single method has gained wide acceptance for use in clinical routine, so the muscle noise problem remains unsolved in ECG signal processing (Sörnmo & Laguna, 2005).

## 2.2 QRS complex detection

The following step in the ECG signal processing consists on the detection of all heartbeats in the ECG recording. Due to the QRS complex has generally greater amplitude and higher signal to noise ratio than P and T waves (*see Fig. 1*), the heartbeats identification is usually carried out with a QRS detector. Moreover, the QRS complex has a higher frequency content which can be distinguish from low frequency of P and T waves (Thakor et al., 1984). The QRS detector must be able to detect a large number of different QRS morphologies in order to be clinically useful and able to follow sudden or gradual changes of the cardiac rhythm. Consequently, the performance of any ECG automatic analysis system depends on a correct detection of all QRS complexes in the ECG record.

In the literature, it has been proposed several QRS detectors. Köhler et al., produced a rather comprehensive review of the main QRS detecting algorithms (Köhler et al., 2002). One of them, widely used, was proposed by Pan & Tompkins (Pan & Tompkins, 1985). Its implementation is simple reaching high levels of sensitivity and predictivity (both > 99.5%). Bandwidth, slope and pulse duration are the three criteria used by the algorithm. A bandpass filter keeps the spectral portion where most of the QRS energy concentrates, attenuating the P and T waves low frequency components, removing baseline slow changes or drifts and reducing 50/60 Hz line interference and EMG high frequency noise. A differentiator picks out the steep QRS edges, obviously much different that the other components smoother edges. Thereafter, the mean quadratic value of each signal sample is computed by a non-linear unit to obtain only positive values and to emphasize the QRS high frequency components. A moving window integrator adds up the areas under the quadratic signal to produce pulses and to remove short duration artifacts. Such output goes to the decision unit where each pulse is compared to the preestablished threshold singling it out or not and locating it in its proper relative temporal place. The overall output is composed of the temporal marks or spikes, each corresponding to the detected QRS complex.

## 2.3 ECG delineation

Since important diagnostic information is contained in the wave amplitudes and time durations of a heartbeat (*see Fig. 1*), wave delineation represents an important step in ECG processing (Sörnmo & Laguna, 2005). Basically, ECG delineation consist on the automatic determination of peaks and time limits of the cardiac waves (QRS complex, P and T-waves). Delineation algorithms usually depart from a previous QRS location and define temporal search windows before and after the QRS fiducial point to seek for the other waves. Once the search window is defined, some technique is applied to enhance the characteristic features of each wave (e.g., its frequency band) in order to find the wave peaks.

The localization of ECG wave onsets and offset is a more difficult task, as the signal amplitude is low at the wave boundaries and the noise level can be higher than the signal itself (Martinez et al., 2004). The classical definition of a wave boundary is the time instant at

which the wave crosses a certain amplitude threshold. Unfortunately, this definition is not adequate for cardiac waves delineation, particularly in ECG records corrupted with baseline wander, so it is not used in practice (Sörnmo & Laguna, 2005).

In order to solve this problem, many delineation algorithms examine the change in the slope of ECG signal to detect the wave limits. Hence, the first derivate of the signal is computed and analyzed with respect to zero crossing and extreme values. This delineation scheme is particularly appropriate to find QRS onset and offset points, due to the steep changes in the slopes of these waves (de Chazal & Celler, 1996, Daskalov & Christov, 1999).

ECG delineation is especially problematic with the estimation of T-wave end boundary, which is often characterized by a very gradual transition to the IL. The delineation of T-wave end is problematic even among cardiologists, which can exhibit differences up to 100 ms (Sörnmo & Laguna, 2005). A correct determination of this endpoint is extremely important for an accurate estimation of QT interval (*see Fig. 1*). Different algorithms have been proposed for the automatic detection of T-wave end. Xue & Reddy in 1998 compare the performance of five T-wave delineation algorithms based on: (a) the point at which the T-wave intersects the IL plus a threshold, (b) the point at which the first derivate of T-wave intersects a threshold above IL, (c) the intersection of the maximum slope of T-wave and IL, (d) the intersection of the line fitted by least squares to the maximum slope of T-wave and IL (LSI), and (e) the point at which the T-wave area reaches 90% of its total value. They conclude that LSI method has the best reproducibility (Xue & Reddy, 1998). Other ECG delineation algorithm, based on a multiresolution analysis of ECG signal using dyadic wavelet transform (DWT), has proven to be particularly adequate for a correct estimation of T-wave boundaries (Li et al., 1995, Martínez et al., 2004). This wavelet approach can be viewed as a filter bank of lowpass differentiators with varying cut-off frequencies. The wave boundaries are then found through the different decomposition levels of DWT.

### 3. Indexes of repolarization dispersion based on ECG durations

In this section, we present different VRD indexes obtained from ECG durations. Some of them can measure spatial heterogeneity of repolarization, such as QT dispersion, T-wave width and T-wave peak-to-end duration. Other index, like QT variability can be used to evaluate the dynamic heterogeneity of VR. Also, other spatial heterogeneity indexes, such as, T-wave amplitude, T-wave symmetry and the relationship between T-wave areas, are shortly commented.

#### 3.1 QT interval dispersion

QT dispersion ( $QT_D$ ) is defined as the arithmetic difference between the maximum and the minimum QT interval (*see Fig. 1*) or as QT interval standard deviation between all ECG-leads.  $QT_D$  was first defined on multilead recordings system (Sylvén et al., 1984) and then on the standard 12-lead ECG (Cowan et al., 1988), intended to reflect the duration of the monophasic action potentials (MAPs). Thus, the  $QT_D$  measured on the 12-lead ECG aims to be a non-invasive index of VRD. The main concept proposed by Day et al., which supports the  $QT_D$  as a VRD marker, is the fact that every ECG lead picks up local activity from different heart areas and therefore differences among them directly translate into differences in APD (Day et al., 1990). In consequence  $QT_D$  quickly became popular for its non-invasive nature and calculus simplicity.

In the repolarization analysis, many studies focussed on finding a universal formula that corrected QT (QTc) for heart rate (HR) in every patient (Hodges, 1997). However, Malik et al. showed that the QTc must not be universally applied but individually (Malik, 2002). In this way, animal studies have shown that VRD does not change with HR and need not be corrected for it (Zabel et al., 1997). Also, QT<sub>D</sub> correction in humans can be misleading since changes in this index at different HR may show or reflect modifications in cycle length and not changes in VRD (Subramanian et al., 1999).

Later on, QT<sub>D</sub> was studied by Day et al. in 1992 (see Table 1) under sinus rhythm and controlled ectopic stimulus leading to the conclusion that QT<sub>D</sub> reflected regional variations of the cellular recovery time (Day et al., 1992).

Higham et al. (Higham et al., 1992), found a high correlation between VRD measured on MAPs basis and QT<sub>D</sub> on both sinus rhythm and ventricular pacing. Also Zabel et al., observed that QT<sub>D</sub> was highly correlated to ventricular recovery times and duration of MAPs in isolated rabbit hearts (Zabel et al., 1995). Later on, results were confirmed in humans, comparing QT<sub>D</sub> from ECG 24 hs after MAPs recording, increasing accordingly QT<sub>D</sub> and endocardic MAPs (Zabel et al., 1998b).

Zabel et al., in 32-months follow-up a prospective study including myocardial infarction (MI) patients, failed to find in QT<sub>D</sub> a predictive value of mortality (Zabel et al., 1998a). On the other hand, Mänttari et al., with a 6.5 years follow-up study, did find QT<sub>D</sub> measured to T-wave peak as a predictor of SCD but not of fatal MI (Mänttari et al., 1997).

Using a modified Langendorff-perfused rabbit heart model, Arini et al. compared QT<sub>D</sub> measure from multilead system against the values found when the 12 standard ECG-leads were used. The obtained results supported the importance of multiple recording systems for the evaluation of QT<sub>D</sub> and helped to understand the discrepancies found in clinical applications (Arini et al., 2000). Later, Arini et al., using an animal heart model with multiple electrode recording system, showed a differential behavior in the modulation of VRD depending on whether premature ventricular stimulation (PVS) were elicited at the right or left ventricle. They concluded that different ventricles anisotropic properties, dissimilar wall thickness and fiber orientation partially contribute to the explanation of results (Arini et al., 2001).

More controversial issues came up with Lee et al. (see Table 1), and Macfarlane et al. who simultaneously showed that QT<sub>D</sub> calculated from 12-ECG leads derived from the orthogonal XYZ leads (without any regional information) was similar to that obtained from the standard ECG. Also, Kors et al. (see Table 1), found a high correlation between QT<sub>D</sub> and the parameters of the T-wave loop (T<sub>L</sub>) in the vectocardiogram, concluding that the QT<sub>D</sub> would be more a feature of the T<sub>L</sub> in 3D more than a local VRD phenomenon. If all the repolarization information is contained in the T<sub>L</sub>, then the QT<sub>D</sub> would be a result from the projection effect (Lee et al., 1998; Macfarlane et al. 1998; Kors et al., 1999).

Many technical limitations make QT<sub>D</sub> not reliable. Great efforts have been addressed to define different ways of measurement (Hnatkova et al., 1994a) as well as to analyze their reproducibility (Macfarlane et al., 1998). Kautzner et al. tested that the greater QT intervals in leads displaying greater T-wave amplitudes. They also found a 27-33% interobserver variability for QT<sub>D</sub> whilst a much smaller interobserver variability (2-4%) was found for QT intervals (Kautzner et al., 1994). Lead selection also affects QT<sub>D</sub>. Hnatkova et al. analyzed in a systematic way the measurement errors derived from imperfect sets of leads. Due to the great variability found, they concluded that QT<sub>D</sub> should be compared with a constant and standard set of leads basis (Hnatkova et al., 1994b). On the other hand, Kors & Van Herpen,



postulated a valuable criterion for lead selection based on the frontal leads dependence (Kors & van Herpen, 1998). Another technical problem concerning  $QT_D$  measurement is T-wave end delineation which was before mentioned in Section 2.3. Figure 3 shows  $QT_D$  calculated between two hypothetical ECG leads where it can be seen the difficulties to distinguish between the dispersion generated by estimation error and the real dispersion.

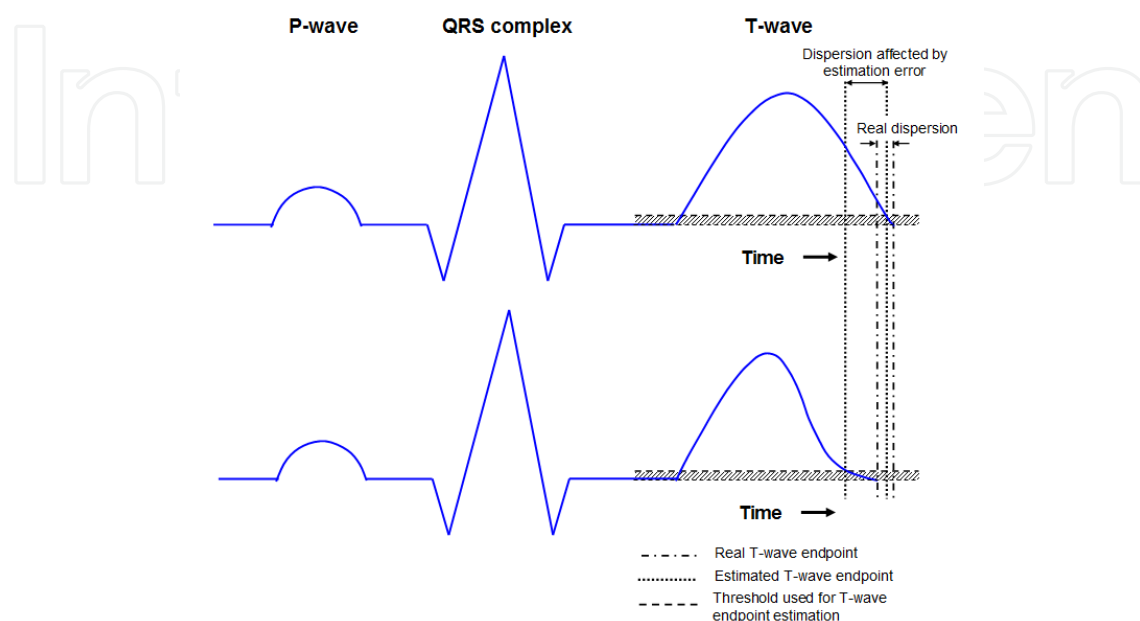


Fig. 3. Both T-waves of the same amplitude have different ends, this results in 'real dispersion' of QT intervals (vertical dashdot lines). Also, from below the threshold level (horizontal dashed lines) defined by an automatic algorithm, there are different proportions of T-waves end (vertical dot lines), this results are called 'Dispersion affected by estimation error' which is different from the 'Real dispersion'.

In spite of the technical limitations and controversies,  $QT_D$  is used in a growing number of medical applications. Examples of this are the assessment of cardiac toxicity in anesthesia (Cafiero et al., 2010) or the search of cardiac indexes in malnourished adults (Hanci et al., 2010).

### 3.2 QT interval variability

In order to separate the heart rate variability (HRV) from the QT variability ( $QT_V$ ), the  $QT_V$  index is redefined as:  $QT_{VI} = QT_V / HRV$ , being this ratio related to arrhythmic events, SCD and heart failure (Berger et al., 1997, Yeragani et al., 2004).  $QT_{VI}$  reflects beat-to-beat changes of the recovery times and such variations in the refractory times can lead to reentrant arrhythmias.

In a prospective study recruiting patients referred to electrophysiological studies, the greater  $QT_V$  belonged to those who presented SCD or ventricular fibrillation (VF) (Atiga et al., 1998). Healthy subjects presented low  $QT_{VI}$  and considerable HRV, with a low average HR and a high average QT, while patients with dilated cardiopathy presented a high  $QT_{VI}$  with low QT average and low HRV with an high HR average.

In 1999, trying to get rid of the T-wave end detection, Courdec analyzed the QT abnormal components in the time-space domain by means of wavelet transform (Couderc et al., 1999) where they found LQTS patients with higher  $QT_V$  than the control patients. Burattini and

Author and year of publication	Short description	Indexes		Conditions for the evaluation of methodologies					
Day et al. (1992)	9 patients under electrophysiological study of palpitation			CI= 300 (ms)			CI= 500 (ms)		
				PSC	VE	FSC	PSC	VES	FSC
		AQT <sub>D</sub> (ms)	22 ±2	80±4	23±6	18±2	87±6	18±2	
Lee et al. (1998)	Conventional and derived ECGs obtain from 129 HS	QT <sub>D</sub> (ms)		40 ±20 (12 leads from XYZ)			41±18 ( from 12 leads)		
Kors et al. (1999)	1220 standard simultaneous 12 ECG leads.	QT <sub>D</sub> (ms)		54.2±27.1 for narrow and large T-wave loop					
				69.5±33.5 for wide and small T-wave loop					
Fuller et al. (2000)	Correlation coefficients of VRD versus T-wave width (T <sub>w</sub> ) and QT <sub>D</sub> for each lead set			Ep	BS	Pc	Op		
		T <sub>w</sub>		0.91	0.84	0.72	0.81		
		QT <sub>D</sub>		0.46	0.47	0.17	0.11		
Arini et al. (2001)	Dispersion Variables (DV) was evaluated as a function of CI and site of stimulation in 12 in vitro rabbit hearts. *p<0.05 vs. 400ms			CI for Stimulus RV (ms)			CI for Stimulus LV (ms)		
				400	250	ERP +5	400	250	ERP +5
		DV (ms)	SDJT <sub>p</sub>	9.6±0.88	10.2±0.84	14.9±0.73*	7.7±0.55	6.2±0.55*	11±1.16*
			SDJT <sub>e</sub>	7.6±0.55	8.1±0.7	11±0.83*	7.1±0.52	4.6±0.72*	11±0.86*

AQT<sub>D</sub> (Adjusted QT<sub>D</sub>)= (maxQT<sub>D</sub> - minQT<sub>D</sub>)/√ n° of leads; CI (Coupling interval); PSC (Preceding Sinus Complex); VE (Ventricular Extrasystole); FSC (Following Sinus Complex); Ep (Epicardial); BS (Body Surface); Pc (Precordial); Op (optimal); SD (Standard Deviation); JTp (J point to T-wave peak); JTe (J point to T-wave end) RV (Right Ventricle); LV (Left Ventricle); ERP (Effective Refractory Period). HS (healthy subjects)

Table 1. Some of the principal results of ECG duration indexes explained in Section 3.

Zareba, on the other hand, proposed a temporal method to measure beat-to-beat QT<sub>v</sub> consisting on correlating T-waves with a pattern (Burattini & Zareba, 1999). This index was validated with ischemic myocardopathy who presented a higher index than control patients. Nevertheless, no correlation with left ventricular ejection fraction (LVEF), HR, HRV and QTc were found.

Almeida et al. in 2006 postulated a parametric linear model to explore interactions between QT<sub>v</sub> and HRV. The method was applied to simulated series and artificial ECG signals, but validated on real ECG data from healthy subjects, where it was found a 40% of QT fraction not correlated with HRV, suggesting that an important part of QT<sub>v</sub> is not linearly driven by HRV and may contain complementary information (Almeida et al., 2006).

Recently, it was shown the relationship between  $QT_{VI}$  and cardiac sympathetic activity in hypertensive patients (Baumert et al., 2011).

### 3.3 T-wave duration

Fuller et al., in 2000 used isolated-perfuse canine hearts (*see Table 1*) to measure  $QT_D$  and T-wave width ( $T_W$ ) from the root-mean-square (RMS) curve obtained from: the available epicardial electrograms, ECG body surface leads, standard precordial ECG leads, and optimal lead set. They induced myocardial VRD by three different ways: changing temperature, modifying the cycle length and changing activation sequence. The VRD, which was measured directly using epicardium recovery times, was compared to  $T_W$  and  $QT_D$ . VRD was strongly correlated with  $T_W$  computed from the RMS series, but not with  $QT_D$  (Fuller et al., 2000).

Arini et al., proposed that T-wave widening can result from a result of combined dispersion between apex-base and transmural APD heterogeneities. They used the addition of antiarrhythmic drugs and PVS to induce increase VRD in an In Vitro rabbit heart model (*see Table 1*), concluding that VR is reflected in the ECG as a  $T_W$  widening, while index  $QT_D$  failed as risk stratification (Arini et al., 2008a).

Other studies have shown T-wave peak-to-end ( $T_{PE}$ ) interval as a measure of transmural dispersion (Zareba et al., 2000), although it is difficult to associate this concept with the ECG standard, since the concept of  $T_{PE}$  is mainly associated to the ECG derived from the Wedge preparation (Antzelevitch et al., 1999). In addition, the  $T_{PE}$  can replace the  $T_W$  to measure dispersion during ischemia, since the measurement of T-wave onset is very unstable during ST-segment modifications (Arini et al., 2008b).

## 4. Indexes of repolarization dispersion associated to ECG-morphology

In this section, we present VRD indexes obtained from ECG morphology changes. These indexes are based on the hypothesis that morphological changes on the T-wave will appear when VRD is increased. The indexes complexity of repolarization, T-wave residuum, the total cosine R-to-T, the T-wave morphology dispersion, T-wave area and T-wave amplitude, can measure spatial heterogeneity of repolarization. Other indexes from beat-to-beat, such as micro T-wave alternans and T-wave spectral variance can measure dynamic heterogeneity of VR.

### 4.1 Evaluation of T-Wave morphology employing Singular Value Decomposition

The main technique used to evaluate morphological or energy changes of T-wave during increased VRD is the Singular Value Decomposition (SVD). SVD is a mathematical transformation based on the correlation between signals. In this case, SVD is applied to the eight mutually independent leads (I, II, V1-V6) and then the information is reconstructed in an optimal orthogonal space of eight pseudo-leads (S1-S8) (*see Fig. 4*). In the new space, S1 will have the maximal energy or eigenvalue ( $\lambda_1$ ) in this direction, S2 will contain the maximal energy ( $\lambda_2$ ) perpendicular to S1, S3 will have the maximal  $\lambda_3$  perpendicular to the two first pseudo-leads and so on. S1, S2 and S3 have the 98% of total ECG energy approximately, and are named dipolar components ( $C_D$ ) ( $\lambda_1, \lambda_2, \lambda_3$ ), whereas S4-S8 have the 2% residual and are called non-dipolar components ( $C_{ND}$ ). The  $C_D$  is the ECG energy represented in 3D, and shows the normal activity, but for  $C_D$  are not enough to represent pathological activity adequately, being necessary the  $C_{ND}$ .

The Complexity of Repolarization ( $C_R$ ) index is represented by the ratios between eigenvalues (Priori et al. 1997). In normality conditions, the  $T_L$  can be represented like a 3D vector with eigenvalues  $\lambda_1 \lambda_2 \lambda_3$  relative to the principal axes  $S_1 S_2 S_3$ . In general,  $T_L$  is concentrated in the  $\lambda_1$  and  $\lambda_2$  values denominated preferential plane and it can be quantified by  $C_R$  like a narrow or a rounded loop in this plane. Furthermore, the planarity can be calculated, because in a loop totally plane  $\lambda_3$  is equal to zero.

The ventricular gradient is the resulting vector of all the instantaneous vectors of depolarization and repolarization. Expanding this concept, it can be estimated the wavefront direction descriptor, named Total cosine R-to-R ( $T_{CRT}$ ). This index was defined like the cosine of the angle formed between the dominant vectors of the VR and depolarization, measured in a 3D loop of SVD space (Acar et al., 1999). Also, the T-wave morphology dispersion ( $T_{MD}$ ) index measures dissimilarities of the T-wave shapes between different leads and reconstruction vectors of the individual ECG leads and it is calculated as the average of angles among pairs of reconstruction vectors (Zabel & Malik, 2004). Finally, the T-wave residuum ( $T_{WR}$ ) index was proposed by Malik et al., and estimates the non-dipolar components relative energy. The  $T_{WR}$  can be absolute ( $T_{WRa}$ ) defined like  $C_{ND}$  and relative ( $T_{WRr}$ ), the  $T_{WRa}$  normalized by total energy (Malik et al, 2000).

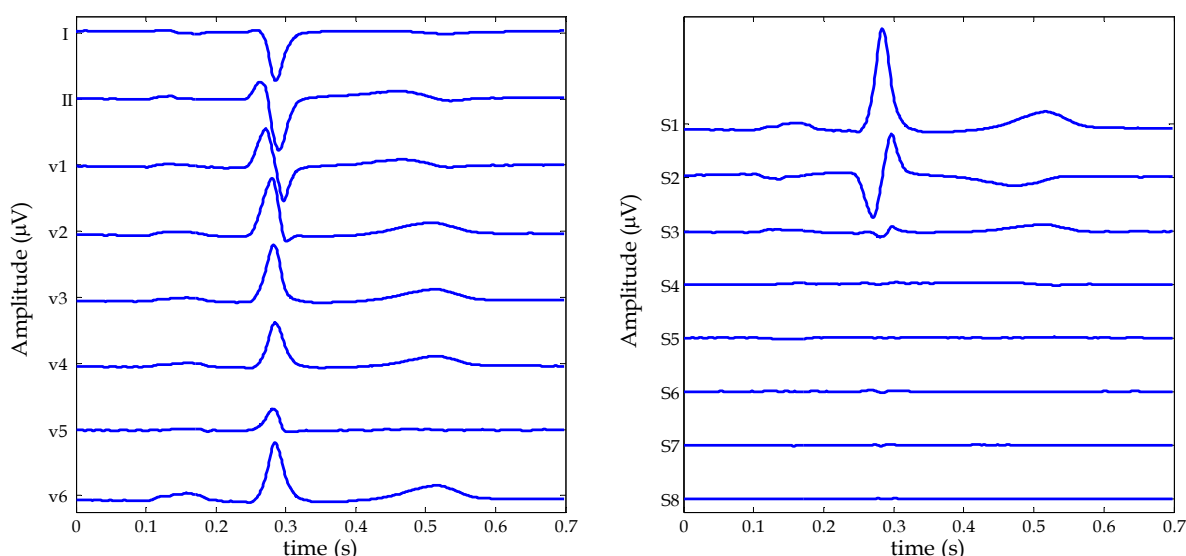


Fig. 4. Standard ECG (left panel) and pseudo-leads obtained from ECG SVD (right panel).

Badilini et al. applied the relationship between 3D  $T_L$  morphology and scalar  $QT_D$ . This analysis was applied to the XYZ ECG obtaining the normalized eigenvalues with the aim to estimate one loop narrowness parameter and two planarity parameters. They evaluated the parameters in healthy subjects (HS) and post MI and LQTS patients. The scalar measurements were significantly larger in patients with MI and LQTS than in HS but only in 3D analysis was observed a loss of planarity and an increased roundness of the  $T_L$ , differentiating MI from LQTS patients. They concluded that the spatial nature of  $T_L$  was associated to scalar interlead variability (Badilini et al., 1997).

Almost simultaneously, Priori et al. applied eigenvalues relationship to 12-lead Holter recordings (see Table 2.) to estimate the  $C_R$ , and compared their results against other methods that characterize QT interval. They found that the ratio of the  $\lambda_2$  to  $\lambda_1$  was more representative of  $C_R$ , being  $C_{R24h}$  the average of  $C_R$  in 24 hs. They observed that  $C_{R24h}$  was

significantly higher in LQTS than in HS. They concluded that eigenvalues relationship can be used to quantify the  $C_R$  in a non invasive way (Priori et al., 1997). In addition to those indexes previously described, Acar et al. developed another indexes linked to  $T_L$ . They employed ECG records with HS and hypertrophic cardiomyopathy (HCM) (see Table 2) to calculate the conventional measures of VR and the ratios among eigenvalues. They concluded that new descriptors were more reproducible than the conventional QT interval descriptors and  $T_{MD}$  and  $T_{CRT}$  indexes were the best indexes for discrimination between groups (Acar et al., 1999).

Author and year of publication	Short description	Indexes	Conditions for the evaluations of methodologies			
Priori et al., (1997)	Were studied 36 LQTS patients and 40 control subjects.		Normal	LQTS	Sen %	
		QTc (ms)	414±18	514±59	88	
		QT <sub>DC</sub> (ms)	38±9	82±37	69	
		C <sub>R24h</sub>	13±3	34±12	88	
Acar et al., (1999)	Were employed 76 normal subjects and 63 patients with HCM. p-value of separation between normal and HCM for each index evaluated		Normal	HCM	p- value	
		T <sub>MD</sub>	10.72±4.784	41.1±26.85	2.818x10 <sup>-18</sup>	
		T <sub>CRT</sub>	0.522±0.274	-0.351±0.522	3.548x10 <sup>-19</sup>	
		λ <sub>2</sub> /λ <sub>1</sub>	15.56±6.162	23.56±10.85	9.886x10 <sup>-7</sup>	
		λ <sub>3</sub> /λ <sub>1</sub>	4.826±2.373	7.765±4.235	6.603x10 <sup>-9</sup>	
Malik et al., (2000)	The study was realized with a group of 78 HS, 68 HCM, 72 DCM and 81 acute MI patients.		Normals	HCM	DCM	acute MI
		QT <sub>D</sub> (ms)	33.6±18.3	47±19.3	37.8±21.2	57.5±25.3
			Normals vs DCM: NS, other p<0.009			
		T <sub>WR</sub> (%)	0.029 ±0.031	0.067 ±0.067	0.112 ±0.154	0.186 ±0.308
			HCM vs DCM: NS, other p<0.006			
Arini et al., (2008a)	The experiments were carried out in 20 isolated rabbit hearts during PE and after DS	QT <sub>D</sub> and T <sub>WR</sub> correlation	-0.0446	0.2805	-0.1531	0.0771
			p=0.03 for HCM , other NS			
			Control	PVS	Control	DS
		T <sub>W</sub> (ms)	78±10.3	118.5 ±15.7	78±10.3	95.2±7.9
		SDQT (ms)	7.6±2.2	13±3.4	6.5±1.4	11.6±1.9
		θ <sub>PT</sub> (°)	137±65	129±61	35±51	117±49

NS (non significant); QT<sub>DC</sub> (QT dispersion corrected); SD (Standard Deviation).

Table 2. Some relevant results from ECG SVD and the comparison with another indexes



A research in which  $QT_D$  and  $T_{WR}$  was calculated in 12-lead resting supine ECGs records corresponding to HS, HCM patients, dilated cardiomyopathy patients (DCM) and survivors of acute MI (*see Table 2.*) was carried out by Malik et al. They concluded that  $C_{ND}$  differ in clinically well-defined groups, and that  $QT_D$  is unrelated to them, so,  $QT_D$  is not a direct measure of local VRD (Malik et al., 2000).

Zabel et al., during a prospective study for risk stratification in post-MI patients evaluated  $C_R$ ,  $T_L$  dispersion ( $T_{LD}$ ),  $T_L$  area,  $T_{CRT}$  and  $T_{MD}$ , and where correlated with  $QT_D$  and clinical data. Zabel et al. found that  $T_{CRT}$  and  $T_{LD}$  is suitable for risk discrimination. They realized a multivariate analysis including other predictive risk stratifiers. They concluded that T-wave morphology analysis can be used in the post-MI risk estimation and in combination with other risk markers enhanced the final results (Zabel et al., 2000). Later, Zabel et al. presented a study to assess the prognostic value of the same parameters evaluated in 2000, adding the  $T_{WRa}$ ,  $T_{WRr}$  and QT interval in long term survivals in US veterans with cardiovascular disease and the patients were follow up  $10.4 \pm 3.8$  years. They showed that  $T_{WR}$  presents a significant long-term prognostic power in the population studied (Zabel et al., 2001).

The  $C_D$  and  $C_{ND}$  were analyzed by Biagetti et al., in isolated rabbit hearts model. The aim was to analyze the role of both components in the determination of  $T_{WR}$  observing that both increased significantly during PVS and after D-sotalol (DS) exposure. Despite the increase of  $T_{WRa}$ , the  $T_{WRr}$  decreased during PVS and did not change after DS. They concluded that due to the fact that  $C_D$  and  $C_{ND}$  can change simultaneously,  $T_{WRr}$  may not reflect regional heterogeneity of VR with accuracy and that  $C_{ND}$  of the 2<sup>nd</sup> half of the T-wave can be related to transmural VRD (Biagetti et al., 2004).

A study that analyzed Principal Component Analysis (PCA) parameters in relation to conduction disturbances in patients with chest pain and ECG nondiagnostic of acute MI was developed by Kesek et al. in 2004. They calculated  $C_R$ ,  $T_{WRa}$  and  $T_{WRr}$  which were assessed against clinical and ECG parameters, discharge diagnosis and total mortality during 35-months follow up. They found that a  $T_{WRr}$  increased with conduction disturbances, which were associated with augmented VR inhomogeneity (Kesek et al., 2004).

Malik et al. in 2004 carried out a research in which stratified risk of arrhythmic events by mean of LVEF and HR, HRV, the slope of HR turbulence and  $T_{CRT}$  in patients who might benefit from prophylactic antiarrhythmic intervention. It was evaluated individual risk characteristics and the combinations of them. They concluded that  $T_{CRT}$  was a strongest risk stratifier that compared very favorably to LVEF and was also strongest in combination with other stratifiers like LVEF (Malik et al., 2004).

Arini et al., evaluated indexes that quantify the VRD for cardiac risk. The study was carried out in multilead ECG records from animal heart model (*see Table 2.*); employing DS and PVS achieved to increment VRD. They calculated indexes from the absolute ECG summation signal (T-wave amplitude, area and width) and from the SVD of the ECG:  $\theta_{PT}$  (angle between the 1<sup>st</sup> SVD axis and the VR axis),  $T_{WR}$ ,  $T_{MD}$ , unnormalized  $T_{MD}$ , and  $T_{CRT}$ . They compared the results with the classical indexes based on QT and concluded that the globally increased VRD can be reflected by  $T_W$  (Arini et al., 2008a).

T-wave morphology parameters were studied in LQTS patients by Anttonen et al. in 2009. They wanted to determine if these parameters presented abnormal value in these patients and whether can be used to diagnose LQTS. They measured  $T_{CRT}$ ,  $T_{LD}$  among others and concluded that patients with short QT interval and with a history of arrhythmic events presented abnormal values of T-wave morphology parameters (Anttonen et al., 2009).

## 4.2 Other T-wave morphology indexes

T-wave amplitude, T-wave symmetry and the relationship between T-wave areas were proposed as markers of cardiac arrhythmogenic. In ischemia, symmetry and amplitude of T-wave changes (Hartikainen, 2004) agreed with a computer model (Di Bernardo et al., 2001) in which this disease was simulated. Studies have found differences in amplitude, area and symmetry of the T-wave stress test (Langley et al., 2002), antiarrhythmic and PVS with respect to control (Arini et al., 2005).

The beat-to-beat variability of VR using QT interval (Section 3.2) approach is largely influenced by criteria used to detect T-wave end point, as was mentioned in Section 2.3. In order to solve this problem, Steinbigler et al. developed the technique of T-wave Spectral Variance ( $T_{WSV}$ ) using the two dimensional Fast Fourier transform. This technique can detect dynamic changes in VR pattern either in amplitude or duration independently of the exact delineation of T-wave end (see Fig. 3). Steinbigler et al. tested  $T_{WSV}$  capacities to detect inhomogeneities of VR in retrospective way of post-MI patients with and without a history of arrhythmias (Steinbigler et al., 1998). Later on, Valverde et al., using an animal model of myocardial infarction, verified the presence of dynamic VR heterogeneity associated with chronic MI and further contributes to identify the infarcted animals (Valverde et al., 2002).

## 4.3 Micro T-wave alternans

The electrical T-wave alternans is defined as a variation in VR morphology on an alternate beat basis (Murda'H et al., 1997) and can be distinguished in macro and micro alternans.

Macro T-wave alternans refers to a systematic or beat to beat alteration in amplitude, width, and/or shape which can be visualized easily in surface ECG. Micro T-wave alternans ( $\mu T_{WA}$ ) is a microscopic alteration of ST-T complex or T-wave, which are revealed through the digital processing of ECG signal (Lux & Brockmeir, 2004) showing dynamic heterogeneity of VR. Experimental and clinical evidence shows that  $\mu T_{WA}$  are linked to abnormal electrophysiological functions and are cardiac risk markers in patient with coronary artery disease (Ikeda et al., 2002; Nearing et al., 1991; Pires 2002; Rosenbaum et al., 1996 as cited in Lux & Brockmeir, 2004) dilated cardiomyopathy (Adachi et al., 1999 as cited in Lux & Brockmeir, 2004), myocardial hypertrophy (Kon-No et al., 2001, as cited in Lux & Brockmeir, 2004) and hypertension (Hennersdorf et al., 2001, as cited in Lux & Brockmeir, 2004). Pastore et al. measured cellular APD employing optical mapping techniques in the epicardial surfaces of guinea pigs revealing more details about  $\mu T_{WA}$  mechanism. They demonstrated that when HR is incremented to critical values, spatial gradients of VR can be developed by neighboring cells membrane repolarization alternating with the opposite phase. This behavior can be detected in surface ECG at microvolt levels and the heterogeneities produced are the cause of regional VRD. Also, these gradients have enough magnitude to induce unidirectional block and reentrant VF (Pastore et al., 1999).

The principal technique used to detect  $\mu T_{WA}$  is spectral analysis and their presence is defined by a magnitude of 1.9  $\mu V$  or greater, the relationship between  $\mu T_{WA}$  and HR and alternans ratio (Bloomfield et al., 2002).

The spectrum depicts the frequencies at which beat-to-beat fluctuations in the amplitude of the T-wave occur. The  $\mu T_{WA}$  is present with a periods generally of two beats (2:1 relationship) and this appears in the spectrum at a frequency of 0.5 cycles per beat (cpb), hence, the magnitude of the peak at this frequency is a direct measure of electrical alternans allowing differentiate it from another signals occurring at other frequencies like noise or the breathing signal (Murda'H et al., 1997).

The measurement of  $\mu T_{WA}$  is highly dependent on HR, appearing when the HR increases above 90 beats per minutes (Bloomfield et al., 2002). The  $\mu T_{WA}$  measurement can be done in a non invasive way during exercise stress testing or in an invasive way during atrial stimulation with the final objective of keeping HR invariant (Constantini, 2004).

Another important feature of spectral analysis is the alternans ratio (AR), whose value represents the number of standard deviation for which the alternans magnitude exceeded the noise level (Bloomfield et al., 2002).

The significant finding was done by Adam et al. between 1981 and 1984 quantifying from a non-invasive way in dogs (*see Table 3*)  $\mu T_{WA}$  to determine the existence of relation between temporal variability of VR and susceptibility to VF, measured with an index called VF Threshold (VFT). The VFT was reduced inducing hypothermia, tachycardia and by coronary artery ligation (CAL). They found that when VFT was reduced, a  $\mu TWA$  pattern was developed. They made an index, T-wave Alternans Index (TWAI), defined as the square root of the amplitude of the power spectrum minus the noise (Adam et al., 1984) and it was called spectral method (SM).

Smith et al., in 1988 quantified the degree and statistical significance of waveform alternation present in the magnitude of the three orthogonal-lead ECG. Smith et al. reported the relationship between electrical alternans and electrical stability that was found in experimental models with dogs and clinical studies (*see Table 3*). The electrical alternans was measured with an index called Alternating Electrocardiographic Morphology Index (AEMI) and electrical stability in dog preparations was assessed via VFT measurement and in the clinical studies via programmed stimulation (Smith et al., 1988).

Nearing et al. in 1991 implemented the Complex Demodulation Method (CDM) which detected the oscillatory nature of ECG signal during  $\mu T_{WA}$ , modeling it like a sinusoidal signal of 0.5 cpb with phase and amplitude variable. The amplitude was estimated demodulating the 0.5 cpb signal components. They revealed that  $\mu T_{WA}$  is concentrated during the first half of the T-wave coinciding with the vulnerable period of cardiac cycle, linking  $\mu T_{WA}$  with vulnerability of VF (Nearing & Verrier, 1991).

Rosembaum et al. in 1994 tested the Smith et al. hypothesis in humans by mean of electrophysiologic studies (*see table 3*). The  $\mu T_{WA}$  was expressed by two indexes Cumulative Alternans Voltage (CAV) defined as the square root of the alternans peak minus the noise mean and the alternants ratio is defined like the ratio between the alternans peak minus the noise mean and the noise standard deviation. The electrophysiologic test was considered positive if sustained Ventricular Tachycardia (VT) or VF was induced after applied extra stimuli. They concluded that  $\mu T_{WA}$  was a significant predictor of inducible arrhythmias on electrophysiologic testing (Rosembaum et al., 1994).

The method proposed by Laguna et al. consists on applying the Karhunen-Loeve Transform (KLT) to each element of an ST-T vector. Then they calculated the Power Spectral Density (PSD) of the KLi series by the FFT during fixed periods of time. Finally the power band is estimated in those bands around the frequency where alternans appear (0.5 and 0.25cpb). The  $\mu TWA$  is detected when a threshold is exceed. This robust method was validated using simulated and real ECG recordings (Laguna et al., 1996).

Burattini et al. in 1997 performed a time domain Correlation Method (CM) for  $\mu T_{WA}$  detection and compared it with the SM using simulation data. They analyzed the ability of these methods to detect non-stationary  $\mu T_{WA}$  and  $\mu T_{WA}$  under different factors which affect

Author and year of publication	Short description	Index or indication of $\mu T_{WA}$	Conditions for the evaluations of methodologies		
Adam et al. (1984)	The experiments were performed in 20 dogs	TWAI	<i>Hypothermia</i>	<i>Tachycardia</i>	<i>CAL</i>
			(7e.) 7/7 VFT↓ p<0.03 6/7 TWAI↑ p< 0.03	<i>Epicardial ECG</i> (6 e.) 6/6 TWAI↑ p< 0.02	<i>Epicardial ECG</i> (11 e.) 11/11 TWAI↑ p< 0.001
				<i>Surface ECG</i> (10 e.) 07/10 TWAI↑ p< 0.09	<i>Surface ECG</i> (10 e.) 07/10 TWAI↑ p< 0.08
Smith et al. (1988)	The experiments were performed in 10 dogs	AEMI (ST-T)	<i>Hypothermia</i>	<i>Transient occlusion of the LAD</i>	
			(10 e.) 10/10 AEMI↑ p<0.0001	(10 e., 24 m) 17/24 AEMI↑ p<0.002	
	23 studies to predict inducibility of VT or VF	Presence or absence of alternation	Alternation identify the inducible population with <i>Sen.</i> : 92 % and <i>Spec.</i> : 50% p< 0.05		
Rosembaum (1994)	83 patients examined to evaluate if levels of $\mu T_{WA}$ predicted vulnerability to arrhythmia. 66 patients were follows up for 20 months		<i>General analysis</i>	<i>Patients follow up</i>	
		AR>2.5	<i>Sen.</i> : 81 %, <i>Spec.</i> : 84% p< 0.001	$\mu T_{WA}$ and inducibility of ventricular arrhythmias, significant predictors of survival without arrhythmia p<0.001	
		CAV>10 ( $\mu V$ )	<i>Sen.</i> : 80 %, <i>Spec.</i> : 79% p< 0.003		
Nearing & Verrier (2002)	Simulated ECG and studies in 13 dogs with CAL to assess vulnerability to VF	Not specified	<i>Simulation Studies</i>	<i>Experimental Studies</i>	
			The tests present a $\rho= 0,999$ indicating precision in $\mu T_{WA}$ detection	Revealed vulnerability to MI-induced VF <i>Sen.</i> : 100 %, <i>Spec.</i> :100 %	

The expression x/z means x experiments (e) or measures (m) achieve a result from z experiments or measures made in total. Abbreviations employed in the table: Sen( Sensibility), Spec (Specificity),  $\rho$  (correlation coefficient), isch. (ischemic), CAL (Coronary Artery Ligation), LAD (left anterior descendent)

Table 3. Some relevant results for TWA



real ECG records. The study proved that SM is not adequate for detecting non-stationary  $\mu T_{WA}$ , and while both methods are suitable to detect  $\mu T_{WA}$  in noise presence, with CM were obtained better results (Burattini et al., 1997). In 1999 CM was applied to ECG Holter records from LQTS patients and healthy subjects (Burattini et al., 1999).

Martínez et al. in 2000 evaluated the CDM and CM before mentioned and proposed two alternative methods, one of them was a variation of CDM called Capon Filtering Method (CFM) and the other one based on the KLT. CFM consisted on the replacement of the deterministic filter by a data dependent Capon filter. In addition, Martinez et al. proposed transform the ST-T complex by means of KLT and then apply the CFM. The evaluation of the different detectors was carried out using simulated and real data. This study concluded that CM performed worse than the other methods, which showed a similar performance, having the method that employ KLT and CFM higher computational complexity (Martinez et al., 2000).

In 2002 was proposed a new method to analyze  $\mu T_{WA}$  called Modified Moving Average (MMA) (see Table 3). This one consists on dividing the beats in even beats (A) and odd beats (B) and making a moving average for A and another for B. The  $\mu T_{WA}$  is determined like the maximum absolute difference between A and B MMA within the ST segment and T-wave region. They concluded that MMA is better than CDM because the MMA signal processing features are superior to CDM which can be affected by artifacts (Nearing & Verrier, 2002).

A work published in 2002 by Martínez & Olmos showed that the SM and CDM can be interpreted like a Generalized Likelihood Ratio Test (GLRT) for detection of  $\mu T_{WA}$  and tried to prove that Laplacian distribution is more appropriate to model the noise in  $\mu T_{WA}$  than Gaussian. For this they developed a Laplacian Likelihood Ratio (LLR) method which looked for estimate  $\mu T_{WA}$  with the maximum likelihood estimator (MLE) and detect them employing a GLRT. LLR for Laplacian noise was tested with simulated data and founding that LLR is more robust than SM and CDM but the results obtained were not as significant as was expected (Martínez & Olmos, 2002). In 2003 they employed this model with nonstationary noise obtaining similar results (Martínez & Olmos, 2003).

Monasterio & Martínez in 2009 developed a multilead scheme (MS) in which combined LLR with PCA comparing it with a single-lead (SLS) approach in which detected  $\mu T_{WA}$  lead by lead using Laplacian GLRT and alternans estimation is achieved with MLE (Martínez & Olmos, 2002). The MS consists on finding the eigenvectors matrix applying PCA to the output of a detrending filter which input was a data matrix, obtaining the transform leads and  $\mu T_{WA}$  detection is achieved applying Laplacian GLRT to them. The MS was tested with simulated data and showing better results with a lower SNR than the SLS. Moreover both methods were applied on stress ECG records in healthy and ischemic patients. With MS better results were obtained (Monasterio et al., 2009). In 2010 they presented a MS based on periodic component analysis ( $\pi$ CA) concluding that the new  $\pi$ CA MS detect most efficiently than the MS detector based on PCA, and the SLS approach (Monasterio & Martinez, 2010)

## 5. Conclusions

It has been proposed in the literature several indexes to quantify heterogeneity of VR using surface ECG. These indexes could be divided into two groups: those based on ECG duration and those founded on ECG morphology. Also, in general, these indexes can be used to evaluate: a) In an individual beat simultaneously recorded leads (spatial heterogeneity) which can be calculated as:  $QT_D$ ,  $T_W$ ,  $T_{PE}$ ,  $C_R$ ,  $T_{CRT}$ ,  $T_{MD}$ ,  $T_{WR}$ , T-wave area and



T-wave amplitude or b) in a sequence of beats (dynamic heterogeneity) which can be calculated as:  $QT_V$ ,  $T_{WSV}$ , and  $\mu T_{WA}$ .

The nature of the relationship between  $QT_D$  and VRD is controversial, as was showed in Fig. 3. First, due to technical issues, involving the determination of the T-wave end, the existence of U-wave and notched T-waves, as was showed in Fig. 3. Second, the problems with determining increased heterogeneity of VR using  $QT_D$  are the effects generated by the projections of  $T_L$  that have different shapes and different angles onto the axis of each ECG lead, which results in T-waves that have different amplitudes and morphologies. That is how to emerge the necessity to find indexes that allow study another aspects of VR and characterize their anormalities, solving at the same time the problems with measures in the time-domain transforming the ECG signals to another domain obtained by SVD (see Fig. 4).

$C_R$  has been evaluated in different cardiac pathologies. This index was employed using 12 standard ECG-lead and, although certain commercial equipment include it, its role in diagnostic is not well defined. In general, the T-wave morphology indexes, such as,  $T_{CRT}$ ,  $T_{MD}$ ,  $T_{WR}$ ,  $T_{WSV}$ , have detected medium and high cardiac risk, however, the association between pathological mechanisms and these indexes still need further study.

In another sense, the  $T_W$  evaluated from RMS curve or absolute ECG summation signal, could measure apex-base or transmural VRD or both simultaneously, but it is necessary to study these parameters in different cardiac conditions. Although,  $T_{PE}$  was measured in a few clinical studies, the results are controversial. While T-wave symmetry and the relationship between T-wave areas has been proposed like cardiac risk markers (Zareba et al., 2000), its use is not widespread.

The  $\mu T_{WA}$  index have shown as a promising risk stratification index of SCD in some clinical populations, and as an important marker of cardiac electrical instability linking  $\mu T_{WA}$  with VRD and ventricular arrhythmias. Despite this, there are still technical limitations in the determination of  $\mu T_{WA}$  and controversy about its clinical validity under certain circumstances. On the other hand, there are a lot of techniques which detect and measure  $\mu T_{WA}$ , but have not been standardized the optimal times, conditions and methods for the measurement of  $\mu T_{WA}$ . Also,  $\mu T_{WA}$  has not been evaluated in combination with other markers of SCD risk. All these aspects not covered yet, can be explored in future studies.

In conclusion, some indexes presented and evaluated in this chapter have restricted capacity to predict cardiac risk, and others have shown potential but still need to validate in medical practice. Also most of them have been evaluated in small patient populations and some of them only in animal models. Hence, in general, it should be carried out more tests for their implementation in the clinical practices. Finally, it would be important an expert consensus to unify criteria for assessment of the parameters to evaluate VRD in the same way that was done for another ECG computational techniques like late potentials in high-resolution ECG (Breithardt et al., 1991) or heart rate variability, (Heart rate variability-Standard, 1996) for which have been developed several standard documents by specialized committees.

## 6. Acknowledgements

This work has been supported by Consejo Nacional de Investigaciones Científicas y Técnicas (PIP 538) and Agencia Nacional de Promoción Científica y Tecnológica (PICT 2108), both institutions from Argentina.

## 7. References

- Acar, B., Yi, G., Hnatkova K. & Malik M. (1999). Spatial, temporal and wavefront direction characteristics of 12-lead T-wave morphology. *Medical & Biological Engineering & Computing*, Vol.37, pp. 574- 584, ISSN 0140-0118
- Adam D., Smith J., Akselrod S., Nyberg S., Powell A. & Cohen R.(1984). Fluctuations in T-Wave Morphology and susceptibility to ventricular fibrillation. *Journal of Electrocardiology*, Vol.17, pp. 209- 218, ISSN 0022-0736
- Almeida R., Gouveia S., Rocha A., Pueyo E., Martinez J. & Laguna (2006). QT Variability and HRV interactions in ECG: quantification and reliability. *IEEE Transactions on Biomedical Engineering*, Vol. 53, No. 7, pp 1317-1329, ISSN 0018-9294.
- Amlie J. (2000). Increased dispersion of repolarization: A major mechanism behind the genesis of malignant ventricular arrhythmias in cardiac diseases. In: *Dispersion of ventricular repolarization: State of the art*, Olsson S., Amlie J., Yuan S. (Editors), pp. 143-163, Futura Publishing Company, Inc., ISBN 0-87993-458, Armonk, New York
- Anttonen O., Junttila J., Giustetto C., Gaita F., Linna E., Karsikas M., Seppänen T., Perkiömäki J., Mäkitallio T., Brugada R. & Huikuri H. (2009). T-Wave morphology in short QT syndrome. *Annals of Noninvasive Electrocardiology*, Vol. 14, No. 3, pp. 262-267, ISSN 1082-720X
- Antzelevitch C., Shimizu W., Yan G., Sicouri S., Nesterenko W., Burashnikov A. ,Di Diego J., Saffitz J., & Thomas G. (1999). The M cell: Its contribution to ECG and to normal and abnormal electrical function of the heart. *Journal of Cardiovascular Electrophysiology*, Vol. 10, pp. 1124-1152, ISSN 1045-3873
- Arini P., Bertrán G., Valverde E. & Laguna P. (2008a). T-wave width as an index for quantification of ventricular repolarization dispersion: Evaluation in an isolated rabbit heart model. *Biomedical Signal Processing and Control*, Vol. 3, pp. 67-77, ISSN 1746- 8094
- Arini P., Baglivo F, Martinez J. & Laguna P. (2008b). Ventricular repolarization dispersion during ischemia course measured by temporal and spatial electrocardiographic parameters. *Computers in Cardiology*, Vol. 35, pp. 323-326, ISSN: 0276-6574
- Arini P., Quinteiro R., Valverde E., Bertrán G. & Biagetti M. (2000). Evaluation of QT interval dispersion in a multiple electrodes recording system vs. 12-leads standard ECG in an In Vitro model. *Annals of Noninvasive Electrocardiology*, Vol. 5, No. 2, pp. 125-132, ISSN 1082-720X
- Arini P., Valverde E., Quinteiro R., Bertrán G. & Biagetti M. (2001). Differential modulation on ECG indexes of dispersion of ventricular repolarization depending on the site of pacing during premature Stimulation. *Journal of Cardiovascular Electrophysiology*, Vol. 12, No. 1, pp. 36-42, ISSN 1045-3873
- Arini P., Valverde E., Bertrán G. & Laguna P (2005). Geometrical and temporal ECG features for quantification of increased ventricular repolarization dispersion in an experimental heart rabbit model. *Computers in Cardiology*, Vol. 32, pp. 89-92, ISSN 0276-6574
- Atiga W.L., Calkins H., Lawrence J., Tomaselli G, Smith J & Berger R (1998). Beat-to-beat repolarization lability identifies patients at risk for sudden cardiac death. *Journal of Cardiovascular Electrophysiology*, Vol. 9, No. 9. pp. 899-908, ISSN 1045-3873

- Badilini F., Fayn J., Maison-Blanche P., Leenhardt A., Forlini M., Denjoy I., Coumel P. & Rubel P. (1997). Quantitative aspects of ventricular repolarization: relationship between three-dimensional T-wave loop morphology and scalar QT dispersion. *Annals of Noninvasive Electrocardiology*, Vol. 2, No. 2, pp. 146-157, ISSN 1082-720X
- Baumert M., Schlaich M, Nalivaiko E., Lambert E., Ika Sari C., Kaye D.M., Esler M., Sanders P. & Lambert G. (2011). Relation between QT interval variability and cardiac sympathetic activity in hypertension. *American Journal of Physiology – Heart and Circulation Physiology*, Vol. 300, No. 4, pp. 1412-1417, ISSN 0363-6135
- Berger R., Kasper E., Baughman K., Marban E., Calkins H. & Tomaselli G. (1997). Beat-to-beat QT interval variability: novel evidence for repolarization lability in ischemic and nonischemic dilated cardiomyopathy. *Circulation*, Vol. 96, No.5, pp. 1557-1565, ISSN 0009-7322
- Bexton R., Vallin H. & Camm A.J. (1986). Diurnal variation of the QT interval-influence of the autonomic nervous system. *British Heart Journal*, Vol. 55, pp. 253-258, ISSN 0007 0769
- Biagetti M., Arini P., Valverde E., Bertrán G & Quinteiro R. (2004). Role of dipolar and nondipolar components of the T wave in determining the T wave residuum in an isolated rabbit heart model. *Journal of Cardiovascular Electrophysiology*, Vol. 15, pp. 356- 363, ISSN 1045-3873
- Bloomfield D., Hohnloser S. & Cohen R. (2002). Interpretation and classification of microvolt T wave alternans test. *Journal of Cardiovascular Electrophysiology*, Vol.13, No.5, pp. 502-512, ISSN 1045-3873
- Breithardt G., Cain M., el-Sherif N., Flowers N, Hombach V., Janse M., Simson M. & Steinbeck G. (1991). Standards for analysis of ventricular late potentials using high-resolution or signal-averaged electrocardiography: a statement by a task force committee of the European Society of Cardiology, the American Heart Association, and the American College of Cardiology. *Journal of the American College of Cardiology* 1991, Vol. 17, pp. 999-1006, ISSN 0735-1097
- Burattini L., Zareba W. & Moss A. (1999). Correlation method for detection of transient T-wave alternans in digital Holter ECG recordings. *Annals of Noninvasive Electrocardiology*, Vol. 4, No. 4, pp. 416-424, ISSN 1082-720X
- Burattini L., Zareba W., Courdec J., Titlebaum E. & Moss A. (1997). Computer detection of non-stationary T wave alternans using a new correlation method. *Computers in Cardiology*, Vol. 24, pp. 657-660, ISSN 0276-6574
- Burattini L. & Zareba W. (1999). Time-domain analysis of beat-to-beat variability of repolarization morphology in patients with ischemic cardiomyopathy. *Journal of Electrocardiology*, Vol.32, pp. 166-172, ISSN 0022-0736
- Cafiero T., Di Minno, R. & Di Iorio, C. (2010). QT interval and QT dispersion during the induction of anesthesia and tracheal intubation: a comparison of remifentanyl and fentanyl. *Minerva Anestesiologica*, Vol. 77, No. 2, pp. 160-165, ISSN 0375 9393
- Costantini O. (2004). Microscopic T wave Alternans, In: *Dynamic Electrocardiography*, Malik M. & Camm J., pp. 439 – 447, Blackwell Futura, ISBN 0-4051-1960-8, USA
- Couderc J., Zareba W., Burattini L. & Moss A. (1998). New method for the quantification of beat-to-beat T wave temporal variability based on interscale changes in wavelet transform of the ECG: Application to simulated ECG signals. *Proceeding of the*

- IASTED international conference on Signal processing and communications, ISBN 0-88986-580-9, Nevada, USA, October, 1998
- Cowan J., Yusoff K., Moore M., Amos P., Gold A., Bourke J., Tansuphaswadikul S. & Campbell R. (1988). Importance of lead selection in QT interval measurement. *American Journal of Cardiology* Vol. 61, No. 1, pp. 83-87, ISSN 0002- 9141
- Daskalov I. & Christov I. (1999). Electrocardiogram signal preprocessing for automatic detection of QRS boundaries. *Medical engineering & physics*, Vol. 21, pp. 37-44, ISSN: 1350-4533
- Day C., McComb J. & Campbell R. (1990). QT dispersion: an indication of arrhythmia risk in patients with long QT intervals. *British Heart Journal*, Vol. 63, No. 6, pp. 342-344., ISSN 0007 0769
- Day C., McComb J. & Campbell R. (1992). QT dispersion in sinus beats and ventricular extrasystoles in normal hearts. *British Heart Journal*, Vol. 67, No. 1, pp. 39-41, ISSN 0007 0769
- de Chazal, P. & Celler B. (1996). Automatic measurement of the QRS onset and offset in individual ECG leads. *Proceedings of the 18<sup>th</sup> Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, ISBN 0-7803-3811-1, Amsterdam, The Netherlands, October, 1996
- Di Bernardo D. & Murray A. (2001). T wave shape in clinical research. *Circulation*; pp.104:e80
- Eagle K. (1994). Images in clinical medicine. Osborn wave of hypothermia. *New England Journal of Physiology*, Vol. 10, pp. 680, ISSN 0028-4793
- Fuller M., Sándor G., Punske B., Taccardi B., MacLeod R., Ershler P., Green L., & Lux R. (2000). Estimation of repolarization dispersion from electrocardiographic measurements. *Circulation*, Vol. 102, pp. 685-691, ISSN 0009 7322
- Hanci V., Ayoglu H., Yurtlu S., Yildirim N., Okyay R., Erdogan G., Sayin E. & Turan I. (2010). An evaluation of P wave dispersion, QT, corrected QT and corrected QT dispersion intervals on the electrocardiograms of malnourished adults. *Anesthesia and Intensive Care*, Vol. 38, No. 1, pp. 122-127, ISSN 0310- 057X
- Hartikainen J. (2004). T wave and QT interval changes related to myocardial ischaemia, In: *Dynamic Electrocardiography*, Malik M., Camm J., (Editors). pp. 380 – 389, Blackwell Futura, ISBN 0-4051-1960-8, USA
- Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). *Circulation*, Vol. 93, pp. 1043-1095, ISSN 0009-7322
- Higham P., Hilton C., Aitcheson J., Furniss S., Bourke J. & Campbell, R. (1992). Does QT dispersion reflect dispersion of ventricular recovery? *Circulation*, Vol. 86(Suppl.), pp. 392-392, ISSN 0009-7322
- Hnatkova K., Kulakowski P., Staunton A., Keeling P., Yi G., Camm A. & Malik M. (1994a). Influence of filtering techniques on the time-domain analysis, diagnosis, and clinical use of signal-averaged electrocardiogram. *Pacing Clinical Electrophysiology*, Vol. 17, No.6, pp. 1107-1117, ISSN 0147 8389
- Hnatkova K., Malik M., Kautzner J., Yi G. & Camm J. (1994b). Adjustment of QT dispersion assessed from 12 lead electrocardiograms for different numbers of analyzed electrocardiographic leads: comparison of stability of different methods. *British Heart Journal*, Vol. 72, No.4, pp. 390-396, ISSN 0007 0769



- Hodges M. (1997). Rate correction of the QT interval. *Cardiac Electrophysiology Review*, Vol. 3, pp. 360-363, ISSN 1385 2264
- Huhta J. & Webster J. (1973). 60-Hz interference in electrocardiography. *IEEE Transactions on Biomedical Engineering*, Vol. 20, No. 2, pp. 91-101, ISSN 0018-9294
- Ider Y. & Köymen H. (1995). Removal of power line interference monitoring and reduction in biopotential amplifiers, *IEEE Transactions on Biomedical Engineering*, Vol. 37, pp. 731-735, ISSN 0018-9294
- Janse M., Capucci A., Coronel R. & Fabius M. (1985). Variability of recovery of excitability in the normal and ischaemic porcine heart. *European Heart Journal*, Vol. 6 (suppl), pp. 41-52, ISSN 0195-668x
- Kautzner J., Yi G., Camm J. & Malik M. (1994). Short- and long-term reproducibility of QT, QTc, and QT dispersion measurement in healthy subjects. *Pacing clinical Electrophysiology*, Vol. 17, pp. 928-937, ISSN 0147 8389
- Kawataki M., Kashima T., Toda H. & Tanaka H. (1984). Relation between QT interval and heart rate. Applications and limitations of Bazett's formula. *Journal of Electrocardiology*, Vol. 17, pp. 371-375, ISSN 0022-0736
- Kesek M., Jernberg T., Lindahl B., Xue J. & Englund A. (2004). Principal component analysis of the T wave in patients with chest pain and conduction disturbance. *Pacing and Clinical Electrophysiology*, Vol. 27, pp. 1378-1387, ISSN 0147-8389
- Kligfield P., Lax K. & Okin P. (1996). The QT interval-heart rate relationship during exercise in normal men and women: definition by linear regression analysis. *Journal of the American College of Cardiology* Vol. 28, pp. 1547-1555, ISSN 0735-1097
- Köhler B., Hennig C. & Orglmeister R. (2002). The principles of software QRS detection, *IEEE Engineering in Medicine and Biology Magazine*, Vol. 21, No. 1, pp. 42:57, ISSN 0739-5175
- Koponen H., Alaraisanen A., Saari K., Pelkonen O., Huikuri H., Raatikainen M., Savolainen M. & Isohanni M. (2008). Schizophrenia and sudden cardiac death: a review. *Nordic Journal of Psychiatry*, Vol. 62, No.5, pp. 342-345, ISSN 0803-9488
- Kors J., van Herpen G. & van Bommel J. (1999). QT dispersion as an attribute of T-loop morphology. *Circulation*, Vol. 99, No.11, pp. 1458-1463, ISSN 0009-7322
- Kors J. & van Herpen G. (1998). Measurement error as a source of QT dispersion: A computerized analysis. *Heart*, Vol. 80, pp. 453-458, ISSN 1355-6037
- Kuo C., Munakata K., Reddy P. & Surawicz B. (1983). Characteristics and possible mechanism of ventricular arrhythmia dependent on the dispersion of action potential. *Circulation*, Vol. 67, pp. 1356-1367, ISSN 0009 7322
- Laciar E. & Jané R. (2001). An improved weighted signal averaging method for high-resolution ECG signals. *Computers in Cardiology*, Vol. 28, pp. 69-72, ISSN: 0276-6574
- Laguna P., Ruiz M., Moody G. & Mark R. (1996). Repolarization alternance detection using the KL transform and the beatquency spectrum. *Computers in Cardiology*, Vol.23, pp. 673-676, ISSN 0276-6574
- Langley P., Bernardo D. & Murray A. (2002). Quantification of T wave shape changes following exercise *Pacing and Clinical Electrophysiology*, Vol. 25, pp. 1230-1234, ISSN 0147-8389
- Lee K., Kligfield P., Okin P. & Dower G. (1998). Determinants of precordial QT dispersion in normal subjects. *Journal of Electrocardiology*, Vol. 31 Suppl, pp. 128-133, ISSN 0022-0736



- Li C., Zheng C. & Tai C. (1995). Detection of ECG characteristics points using wavelet transforms. *IEEE Trans Biomed Eng.*, Vol. 42, pp. 21-28.
- Lux R. & Brockmeier K. (2004). Macro T wave alternans, In: *Dynamic Electrocardiography*, Malik M. & Camm J. (Editors), pp. 433 – 438, Blackwell Futura, ISBN 0-4051-1960-8, USA
- Macfarlane P., McLaughlin S. & Rodger, J. (1998). Influence of lead selection and population on automated measurement of QT dispersion. *Circulation*, Vol. 98, No. 20, pp. 2160-2167, ISSN 0009- 7322
- Malik M., Acar B., Gang Y., Yap G., Hnatkova K. & Camm J. (2000). QT dispersion does not represent electrocardiographic interlead heterogeneity of ventricular repolarization. *Journal of Cardiovascular Electrophysiology*, Vol. 11, pp. 835-843, ISSN 1045- 3873
- Malik M., Hnatkova K. & Batchvarov V. (2004). Post infarction risk stratification using the 3-D angle between QRS complex and T-wave vectors. *Journal of Electrocardiology*, Vol. 37, pp. 201-208, ISSN 0022-0736
- Malik, M. (2002). The imprecision of heart rate correction may lead to artificial observations of drug-induced QT interval changes. *Pacing and Clinical Electrophysiology*, Vol. 25, pp. 209-216, ISSN 0147-8389
- Mänttari M, Oikarinen L., Manninen V., & Viitasalo M. (1997). QT dispersion as a risk factor for sudden death and fatal myocardial infarction in a coronary risk population. *Heart*, Vol. 78, pp. 268-272, ISSN 1355-6037
- Martínez J. & Olmos (2003). Detection of T wave alternans in non- stationary noise: a GLRT approach. *Computers in Cardiology*, Vol. 30, pp. 161-164, ISSN 0276- 6574
- Martínez J. & Olmos. (2002). A robust T wave alternans detector based on the GLRT for Laplacian noise distribution. *Computers in Cardiology*, Vol. 29, pp. 677- 680, ISSN 0276- 6574
- Martínez J., Olmos S. & Laguna P. (2000). Simulation study and performance evaluation of T- wave alternans detector. *Proceedings of the 22nd Annual EMBS International Conference*, ISSN 0-7803-6465, Chicago IL, USA, July 23-28, 2000.
- Martínez J., Borges de Almeida R., Olmos S., Rocha A. & Laguna P. (2004). A wavelet-based ECG delineator: Evaluation on standard databases. *IEEE Transactions on Biomedical Engineering*, Vol. 51, No. 4, pp. 570-581
- Monasterio V., Clifford G., Laguna P. & Martínez J. (2010). A multilead scheme based on periodic component analysis for T- wave alternans analysis in the ECG. *Annals of Biomedical Engineering*, Vol. 38, No 8, pp. 2532- 2541, ISSN 0009 6964
- Monasterio V., Laguna P. & Martínez J. (2009). Multilead analysis of T- wave alternans in the ECG using principal component analysis. *IEEE Transactions on Biomedical Engineering*, Vol. 56, No 7, pp. 1880- 1890, ISSN 0018-929
- Murda H M., McKenna W. & Camm J. (1997). Repolarization alternans: techniques, mechanisms and cardiac vulnerability. *Pacing and Clinical Electrophysiology*, Vol.20, pp. 2641- 2669, ISSN 01478389
- Nearing B. & Verrier R. (2002). Modified moving average analysis of T- wave alternans to predict ventricular fibrillation with high accuracy. *Journal of Applied Physiology*, Vol. 92, No. 2, pp. 541- 549, ISSN 8750-7587
- Nearing B., Huang A. & Verrier R. (1991). Dynamic tracking of cardiac vulnerability by complex demodulation of the T wave. *Science*, Vol. 252, pp. 437-440, ISSN 0036 8075

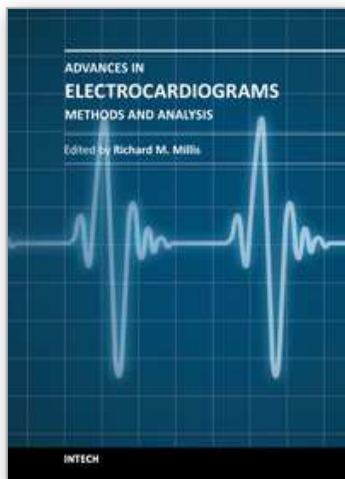
- Pan J. & Tompkins W. (1985). A real-time QRS detection algorithm. *IEEE Transactions on Biomedical Engineering*, Vol. 32, pp 230-236, ISSN 0018-9294.
- Pastore J., Girouard S., Laurita K., Akar F. & Rosembaum D. (1999). Mechanism linking T wave alternans to the genesis of cardiac fibrillation. *Circulation*, Vol. 99, pp. 1385-1394, ISSN 0009-7322
- Pinto V. (1991). Filters for the reduction of baseline wander and muscle artifact in the ECG, *Journal of Electrocardiology*, Vol. 25 (Suppl.), pp. 40-48, ISSN 0022-0736
- Priori S., Napolitano C., Diehl L. & Schwartz P. (1994). Dispersion of the QT interval. A marker of therapeutic efficacy in the idiopathic long-QT Syndrome. *Circulation*, Vol. 89, pp. 1681-1689, ISSN 0009-7322
- Priori S., Mortara D., Napolitano C., Diehl L., Paganini V., Cantù F., Cantù G. & Schwartz P. (1997). Evaluation of the spatial aspects of T-wave complexity in the long- QT syndrome. *Circulation*, Vol. 96, No.9, pp. 3006-3012, ISSN 0009-7322
- Rosembaum D., Jackson L., Smith J., Garan H., Ruskin J. & Cohen R. (1994). Electrical alternans and vulnerability to ventricular arrhythmias. *The New England Journal of Medicine*, Vol.330, No.4, pp. 235- 241, ISSN 0028-4793
- Shimizu W. & Antzelevitch C. (1998). Cellular basis for the ECG features of the LQT1 form of the long QT syndrome. Effects of  $\beta$ - adrenergic agonist and antagonist and sodium channel blockers on transmural dispersion of repolarization and torsades de pointes. *Circulation*, Vol. 98, pp. 2314-2322.
- Shusterman V, Aysin B & Gottipaty V. (1998). Autonomic nervous system activity and the spontaneous initiation of ventricular tachycardia. *Journal of American College of Cardiology*; Vol. 32, pp. 1891-1899, ISSN 0363 6135
- Smith J., Clancy E., Valeri R., Ruskin J. & Cohen R. (1988). Electrical alternans and cardiac electrical instability. *Circulation*, Vol. 77, No. 1, pp. 110-121, ISSN 0009-7322
- Sörnmo L. & Laguna P. (2005). *Bioelectrical Signal Processing in Cardiac and Neurological Applications*, Elsevier Academic Press, ISBN 0-12-437552-9, Amsterdam, The Netherlands.
- Sörnmo L. & Laguna P. (2006). Electrocardiogram (ECG) Signal Processing. In: *Wiley Encyclopedia of Biomedical Engineering*, Metin Akay (Editor), John Wiley & Sons, Inc, Vol. 2, pp. 1298-1313, ISBN 0-471-24967-X.
- Sörnmo L. (1993). Time-variable digital filtering of ECG baseline wander, *Medical & Biological Engineering & Computing*., Vol. 31, No. 5, pp. 503-508, ISSN 0140-0118.
- Steinbigler P., Haberl R. & Steinbeck G. (1998). T wave spectral variance. A new method to determine inhomogeneous repolarization by T wave beat-to-beat variability in patients prone to ventricular arrhythmias, *Journal of Electrocardiology*, Vol. 30, suppl., pp. 137-144.
- Subramanian R., Shalaby A. Campbell R. & Sager P. (1999). Is QT dispersion altered by changes in heart rate? *Journal of American College of Cardiology*, Vol. 33, pp. 113A-114A, ISSN 0735-1097
- Surawicz B. (1997). Ventricular fibrillation and dispersion of repolarization. *Journal of Cardiovascular Electrophysiology* , Vol. 8, pp. 1009-1012, ISSN 1045-3873
- Sylvén J., Horacek B., Spencer C., Klassen G., Campbell, R. & Montague T. (1984). QT interval variability on the body surface. *Journal of Electrocardiology*, Vol. 17, No.2, pp. 179-188, ISSN 0022-0736

- Taback L., Marden E., Mason H.L. & Pipberger H.V. (1959). Digital recording of electrocardiographic data for analysis by digital computer. *IRE Trans Med Electron*, Vol. 6, pp. 167-171, ISSN 0097-1049
- Talmon J., Kors J. & van Bommel J. (1986). Adaptive Gaussian filtering in routine ECG/VCG analysis, *IEEE Transactions in Acoustic, Speech and Signal Processing* Vol. 34, pp. 527-534, ISSN 0096-3518
- Thakor N., Webster J. & Tompkins W. (1984). Estimation of QRS complex power spectrum for design of a QRS filter, *IEEE Transactions on Biomedical Engineering.*, Vol. 31, No. 11, pp. 702-706, ISSN 0018-9294
- Valverde E., Quinteiro R., Arini P., Bertrán G. and Biagetti M. (2002). Beat-to-beat repolarization variability measured by T wave spectral variance index in chronic infarcted animals. *Annals of Noninvasive Electrocardiol*, Vol.7, nro. 4, pp. 319-325.
- Webster J. (1992). *Medical Instrumentation. Application and Design*, J. Webster (Editor), 2nd Edition, Houghton Mifflin Co., ISBN 0-395-59492-8, Boston, USA.
- Weinberg G. (1995). Mechanism of cardiac arrhythmias, In: *Design of cardiac pacemaker*, Webster J (Editor), pp. 35-63, IEEE Press, ISBN 0-7803-1134-5, Piscataway
- Xue Q. & Reddy S. (1998). Algorithms for computerized QT analysis. *Journal of Electrocardiology*. Vol. 30, Suppl 1., pp. 181-186.
- Yeragani, V., Adiga S., Desai N. & Berger R. (2004) Beat-to-beat QT interval variability in atrial fibrillation with and without congestive cardiac failure. *Ann Noninvasive Electrocardiology*, Vol. 9, pp. 304-305, ISSN 0009- 6964
- Zabel M. & Malik M. (2004). Morphological assessment of T wave patterns, In: *Dynamic Electrocardiography*, Malik M. & Camm J., pp. 351 – 357, Blackwell Futura, ISBN 0-4051-1960-8, USA
- Zabel M., Acar B., Klingenhoben T., Franz M., Hohnloser S. & Malik M. (2000). Analysis of 12- Lead T- Wave Morphology for Risk Stratification After Myocardial Infarction. *Circulation*, Vol. 102, (April, 2000), pp. 1252-1257, ISSN 0009-7322
- Zabel M., Malik M., Hnatkova K., Papademetriou V., Pittaras A., Fletcher R. & Franz M. (2001). Analysis of T-wave morphology from the 12- leads electrocardiogram for prediction of long- term prognosis in male US veterans. *Circulation*, Vol. 105, (February, 2002), pp. 1066-1070, ISSN 0009-7322
- Zabel M., Kligenheben T., Franz M.R. & Hohnloser S.H. (1998a). Assesment of QT dispersion for prediction of mortality or arrhythmic events after myocardial infarction. Results of a prospective, long-term follow-up study. *Circulation*, Vol. 97, pp. 2543-2550, ISSN 0009-7322
- Zabel, M., Lichtlen, P.R., Haverich, A. & Franz, M.R. (1998b). Comparison of ECG variables of dispersion of ventricular repolarization with direct myocardial repolarization measurements in the human heart. *Journal of Cardiovascular Electrophysiology*, Vol. 9, No.12, pp. 1279-1284, ISSN 1045-3873
- Zabel M., Portnoy S. & Franz M. (1995). Electrocardiographic indexes of dispersion of ventricular repolarization: an isolated heart validation study. *Journal of American College of Cardiology*, Vol. 25, No. 3, pp. 746-752, ISSN 07351097
- Zabel M., Woosley R. & Franz M.R. (1997). Is dispersion of ventricular repolarization rate dependent? *Pacing and Clinical Electrophysiology*, Vol. 20, pp. 2405-2411, ISSN 0147-8389

- Zareba W., Couderc J. & Mos, A. (2000). Automatic detection of spatial and temporal heterogeneity of repolarization. In: *Dispersion of ventricular repolarization*, Olsson S., Amlie J. & Yuan S. (Editors), pp. 85–107. Futura Publishing Company, Inc., ISBN 0-87993-458, Armonk, New York

IntechOpen

IntechOpen



## **Advances in Electrocardiograms - Methods and Analysis**

Edited by PhD. Richard Millis

ISBN 978-953-307-923-3

Hard cover, 390 pages

**Publisher** InTech

**Published online** 25, January, 2012

**Published in print edition** January, 2012

Electrocardiograms are one of the most widely used methods for evaluating the structure-function relationships of the heart in health and disease. This book is the first of two volumes which reviews recent advancements in electrocardiography. This volume lays the groundwork for understanding the technical aspects of these advancements. The five sections of this volume, Cardiac Anatomy, ECG Technique, ECG Features, Heart Rate Variability and ECG Data Management, provide comprehensive reviews of advancements in the technical and analytical methods for interpreting and evaluating electrocardiograms. This volume is complemented with anatomical diagrams, electrocardiogram recordings, flow diagrams and algorithms which demonstrate the most modern principles of electrocardiography. The chapters which form this volume describe how the technical impediments inherent to instrument-patient interfacing, recording and interpreting variations in electrocardiogram time intervals and morphologies, as well as electrocardiogram data sharing have been effectively overcome. The advent of novel detection, filtering and testing devices are described. Foremost, among these devices are innovative algorithms for automating the evaluation of electrocardiograms.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Ana Cecilia Vinzio Maggio, María Paula Bonomini, Eric Laciár Leber and Pedro David Arini (2012). Quantification of Ventricular Repolarization Dispersion Using Digital Processing of the Surface ECG, *Advances in Electrocardiograms - Methods and Analysis*, PhD. Richard Millis (Ed.), ISBN: 978-953-307-923-3, InTech, Available from: <http://www.intechopen.com/books/advances-in-electrocardiograms-methods-and-analysis/quantification-of-cardiac-ventricular-repolarization-dispersion-using-computarized-ecg->

**INTECH**  
open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821



© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen