Spatio-temporal features of variability repolarization during acute myocardial ischemia

Esteban R. Valverde† Pedro D. Arini†‡

†Instituto de Ingeniería Biomédica, Facultad de Ingeniería, Universidad de Buenos Aires, Argentina
estebanvalverde@hotmail.com
‡Instituto Argentino de Matemática, 'Alberto P. Calderón' CONICET, Buenos Aires, Argentina
pedro.arini@conicet.gov.ar

Abstract— **Several studies have shown that dynamic variability of ventricular repolarization morphology is associated with an increased risk for developing ventricular arrhythmias. We evaluated beat-to-beat ventricular repolarization variability using the T-wave spectral variance (TSV) index during acute myocardial ischemia from the spatial electrocardiogram ECG planes. The study group consisted of 71 patients in which the three orthogonal XYZ leads were obtained during both control (5 min.) and percutaneous coronary intervention (4 min. 36 sec. $\pm$ 80 sec.) of different arteries. Three spatial ECG planes were determined: the frontal plane (FP) defined by XY-leads, the horizontal plane (HP) defined by XZ-leads and the sagittal plane (SP) defined by YZ-leads. Results indicated that the TSV index has shown the most important significant differences with respect to control in: FP to the left anterior descending coronary artery occlusion ($p < 0.001$ in X-lead; $p < 0.0001$ in Y-lead), HP to the right coronary artery occlusion ($p < 0.001$ in Y-lead; $p < 0.0001$ in Z-lead) and SP to the left circumflex coronary artery occlusion ($p < 0.01$ in X-lead; $p < 0.01$ in Z-lead). We conclude that TSV index offers a robust tool for evaluating beat-to-beat repolarization variability during acute ischemia, which depends on the link between the occluded artery and the analyzed ECG plane.**

Keywords— **ECG signal processing, T-wave spectral variance index, 2D-FFT, variability of ventricular repolarization**

1 INTRODUCTION

Ventricular repolarization dispersion (VRD) is a measure of inhomogeneous recovery of excitability during repolarization process. Increments in VRD values that are higher than normal are associated with an increased risk of developing reentrant arrhythmias [1].

Experimental and clinical studies have demonstrated a relationship between VRD and severe ventricular arrhythmia and/or sudden cardiac death [2, 3]. Several techniques have been presented to analyze and quantify the temporal variability of ventricular repolarization [4, 5]. Moreover, beat-to-beat measurement of the QT interval is based on the exact delineation of the T-wave end point, which frequently fails in automatic electrocardiogram (ECG) analysis [6]. The beat-to-beat changes were evaluated by using the T-wave spectral variance (TSV) index method, based on the two-dimensional Fourier transform (2D-FFT), which allows to detect dynamic changes in the repolarization pattern independently of the exact definition of the end point of the T-wave [7, 8, 9]. Steinbigler et al. showed that TSV index reveals an increased VRD in patients prone to ventricular tachycardia and ventricular fibrillation after myocardial infarction, while the corrected QT interval showed no signficant differences [7]. On the other hand, Valverde et al. observed that TSV index detects the presence of temporal repolarization variability in a model of chronic infarcted animals [8]. Later, in another work, Steinbigler et al. showed that TSV index was significantly higher in patients with idiopathic dilated cardiomyopathy prone to ventricular fibrillation with respect to no ventricular fibrillation group [9]. In this work, we have studied the TSV index in the three orthogonal XYZ leads during acute myocardial ischemia induced by percutaneous coronary intervention (PCI). Then, we constructed the spatial ECG planes such as, frontal, horizontal and sagittal planes [10] and we analyzed the TSV index in these ECG planes. Also, we contrasted our results with the results observed by Shenasa et al. in the analysis of ST-segment shift induced by the occlusion of different coronary arteries during percutaneous transluminal coronary angioplasty [11].

As far as we know, there are no results indicating the role of the TSV index from different three spatial ECG planes by other authors. Then the aims of this work were to: 1) Evaluate the presence of beat-to-beat repolarization variability during PCI procedure in the three orthogonal XYZ leads. 2) Determine if there is any preferential spatial ECG plane to detect beat-to-beat variability of ventricular repolarization according to the different occlusion sites.

2 MATERIALS AND METHODS

2.1 Database

In the present work we used a subset of the STAFF III database, which consisted of 71 ECG records from patients at the Charleston Area Medical Center in West Virginia undergoing elective prolonged balloon occlusion during PCI (nonperfusion balloons) in one of the mayor coronary arteries. The study was approved by the local investigational review board, and informed consent was obtained from each subject before enrolment. Eight leads (v1-v6, I, II) were recorded using equipment by Siemens-Elena AB (Solna, Sweden) and digitized at sampling rate of 1000 Hz and amplitude resolution of 0.6 μV. Synthesized three orthogonal XYZ leads were obtained by the Kors transform [12]. The group analyzed was selected from a total of 108 patients, with the condition that T-wave could be delineated during the complete time course of ischemia. Also, we computed the noise/T-wave amplitude ratio (NTR) as the ratio between the total spectral energy from noise bandwidth respect to the total spectral energy of the T-wave [8]. Therefore, those patients with a NTR greater than 0.30 times were considered noisy and rejected. Moreover, those patients who have shown at least one orthogonal XYZ leads with less than 64 consecutive T-waves were rejected.

Finally, the population analyzed consist of 71 patients (48 males, age 60$\pm$12 and 23 females, age 62$\pm$11) , grouped as following: *left anterior descending* (LAD) coronary occlusion artery in 24 patients, *right coronary artery* (RCA) occlusion in 31 patients and *left circumflex* (LCx) coronary occlusion artery in 16 patients. A control recording was acquired continuously for 5 min in supine position prior to the PCI in clinical stable conditions. Then, one continuous ECG was recorded during PCI, 4 min 36 sec with a standard deviation of 80 sec, starting before and ending after balloon inflation and deflation respectively. Therefore, the patients behaved as their own controls.

2.2 ECG preprocessing

We applied a signal pre-processing to the three orthogonal XYZ leads records during control and PCI procedure respectively. Control and PCI procedure records were filtered with a notch filter (Butterworth, 2nd order, 60 Hz) to minimize the power-line interference. A cubic spline interpolation filter was used to attenuate ECG baseline drifts and respiratory artifacts [13]. Thereafter, QRS complexes and their endpoints were detected in each ECG-lead using a modified version algorithm proposed by Pan and Tompkins [14].

In each ECG lead (control and PCI procedure), one QRS template was constructed by calculating the median of the total QRS complexes. After that, if the cross-correlation coefficient between QRS complexes and each QRS template was greater than 98%, a new jitter-corrected QRS complex was obtained, otherwise the complex was rejected. Taken 80 ms from fiducially jitter-corrected QRS endpoint, a T-wave window of 250 ms duration was defined in order to construct an aligned T-waves matrix. This determined the input matrix containing arranged T-waves for the 2D-FFT process.

2.3 T-wave spectral variance index

We have computed the TSV index with an algorithm described by Steinbigler et al. [7] to the three orthogonal XYZ leads for both control and PCI procedure in all the patients. The basement of the algorithm is the 2D-FFT. First, a one-dimensional FFT (1D-FFT) is applied to each T-wave of the T-waves matrix, and the frequency contents was determined. The result is a matrix containing the power spectrum of each T-wave, in which the x-axis correspond to the frequency content in Hertz and the amplitude (z-axis) correspond to the magnitude of the power spectrum expressed in μV^2. A second 1D-FFT is applied to the assembly of the power spectrum of each T-wave in order to evaluate the periodic appearance of each frequency content (y-axis), expressed in cycles-per-beat (cpb), as shown in Figure 1.

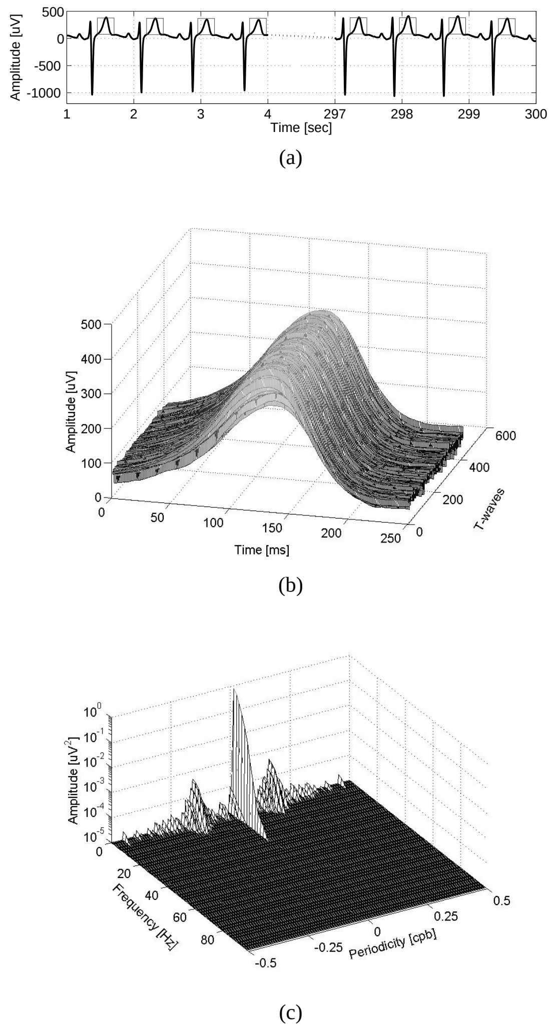


Figure 1: Representative example of calculation of the TSV index. (a) Consecutive T-waves were acquired through 250 msec windows, to build the assembly of the T-waves matrix as shown in (b). In (c), the TSV index was calculated from the 2D-FFT applied to the assembly of T-waves matrix.

Considering T-wave spectral content is less than 50 Hz [9], a non-units (n.u.) TSV index has been calculated as the ratio of the spectral energy with beat-to-beat variability greater than 0 cpb and the total spectral energy, from 0 Hz to 50 Hz.

$$TSV = \left. \frac{\text{Spectral Energy} > 0 \text{ cpb}}{\text{Total Spectral Energy}} \right|_{<50 \text{ Hz}} \tag{1}$$

A TSV index near 0 is indicative of a constant T-wave morphology in all the beats included for the analysis. In contrast, if different degrees of variability in the shape of the T-wave are present, the TSV index tends to 1. Beat-to-beat variability appearing at frequencies from 50 Hz to 100 Hz can be considered as noise because no spectral components of the T-waves appear at these frequencies.

2.4 Statistical analysis

In order to determine the statistical significance of TSV between control situation and PCI procedure, the D'Agostino-Pearson normality test was applied with the aim of quantify the discrepancy between the distribution of TSV index an ideal Gaussian distributions. If the TSV index did not follows a normal distribution, a non-parametric two-sided Mann-Whitney U test was used instead. When *p* value was < 0.05, differences were considered statistically significant. Also, the mean value $\overline{TSV}^C$ of each occlusion site (LAD, LCx and RCA) was obtained for control situation, for each three orthogonal XYZ lead, and similarly, $\overline{TSV}^P$, was calculated for PCI procedure. The results were presented as mean $\pm$ standard error of the mean (SEM).

2.5 TSV index in the spatial ECG planes

Figure 2 shows that the orthogonal XYZ leads can be used to determine three spatial ECG planes respect to heart position: the frontal plane (FP) defined by X and Y leads, the horizontal plane (HP) defined by X and Z leads and the sagittal plane (SP) defined by Y and Z leads. These spatial ECG planes cross each at other at a central point, thus forming a 90° angle against relation each other.

According to Perez Riera et al. [10], who related the XYZ leads with the 12 standard ECG leads, and with the results obtained by Shenasa et al. [11], who investigated the thoracic patterns of ST-segment shift induced by angioplasty; we analyzed and discussed our results. In this sense, we have evaluated the statistical differences between $\overline{TSV}^C$ and $\overline{TSV}^P$ in the frontal, horizontal and sagittal planes by combining the statistical results obtained in the analysis of the orthogonal XYZ leads.

3 RESULTS

From a total of 71 patients subject to balloon inflation procedure in one main coronary artery, the TSV index was calculated both during control situation and PCI procedure for LAD, LCx and RCA patient groups. The TSV index did not follow a Gaussian distribution, consequently a non-parametric two-sided Mann-Whitney U test was used.

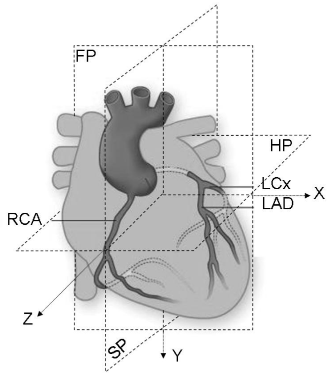


Figure 2: Example of the three spatial ECG planes: frontal (FP), horizontal (HP) and sagittal (SP), constructed from the three orthogonal XYZ leads.

First, we could be observed that the $\overline{TSV}^P$ compared against $\overline{TSV}^C$ was statistically significant for all the three orthogonal XYZ leads. Moreover, as we can see in Fig.3, we performed an analysis of the spatial ECG planes by combining the results as follows:

- The *p*-value of TSV index computed in the X lead *vs.* the *p*-value of TSV index computed in the Y lead, was used to define the frontal plane analysis.

- The *p*-value of TSV index computed in the X lead *vs.* the *p*-value of TSV index computed in the Z lead, was used to define the horizontal plane analysis.

- The *p*-value of TSV index computed in the Y lead *vs.* the *p*-value of TSV index computed in the Z lead, was used to define the sagittal plane analysis.

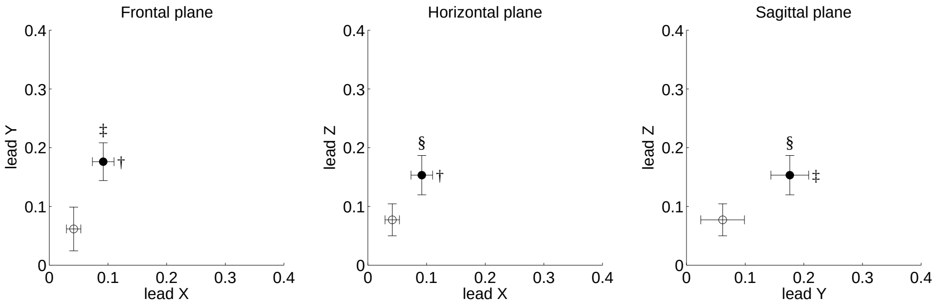
Finally, depending of coronary artery occlusion site, we have selected a preferential spatial ECG plane, basing on the best *p*-value combination.

4 DISCUSSION

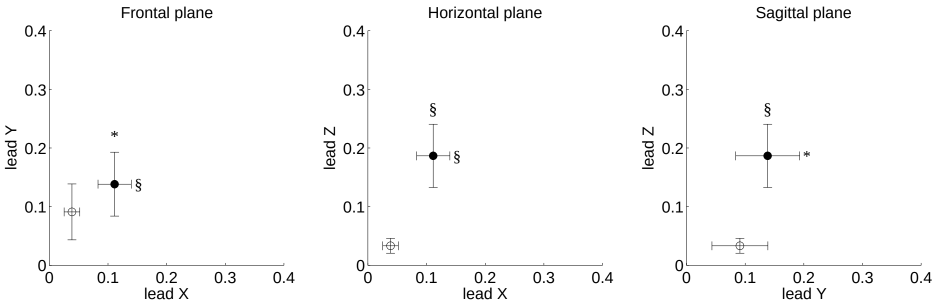
We consider that PCI procedure provides a unique opportunity to examine, in a controlled setting, the ECG alterations produced by a brief coronary artery occlusion to study the electrophysiological changes during acute transmural ischemia [15]. In the present work, the complete coronary occlusion induced by balloon inflation allowed the evaluation of valuable information about spatio-temporal repolarization variability during an ischemia process.

We observed that $\overline{TSV}^P$ compared against $\overline{TSV}^C$ was statistically significant for the three orthogonal XYZ leads in each occlusion site. However, when we analyzed the spatial ECG planes, determined by the three orthogonal XYZ leads, we found some preferential spatial ECG planes according to the different oclussion site.

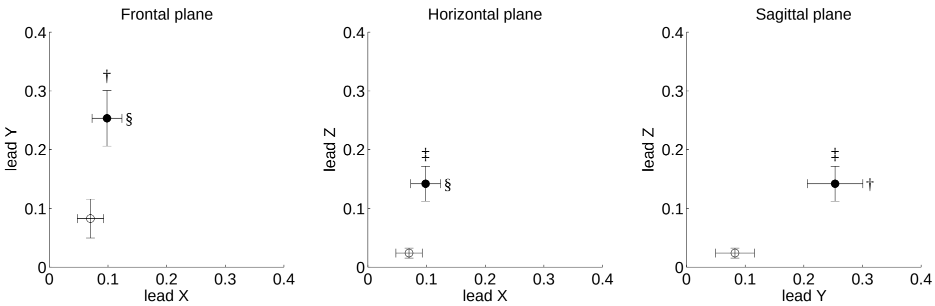
Figure 3a shows that, for LAD occlusion site, both X (it approximately corresponds to I lead, [10]) and Y (it



(a)



(b)



(c)

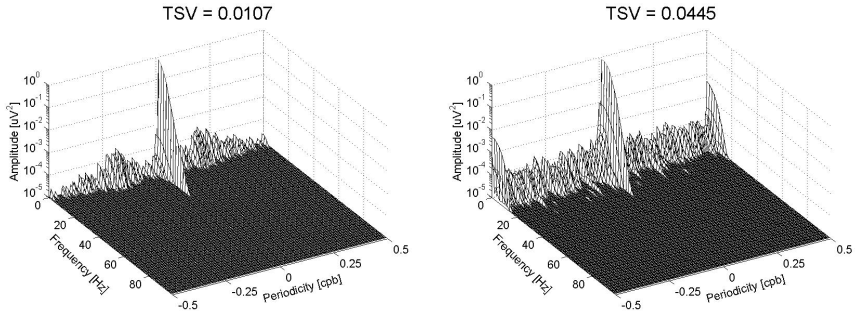
Figure 3: Graphic showing control (○) and PCI procedure (●) TSV indexes, expressed in non-units as $mean \pm SEM$ ($\overline{TSV}$±SEM$\{TSV\}$) for each spatial ECG plane. (a) LAD, (b) LCx and (c) RCA occusion sites. '*' $p < 0.05$, '§' $p < 0.01$, '†' $p < 0.001$, '‡' $p < 0.0001$

approximately corresponds to aVF lead, [10]) orthogonal leads presented the lowest p-values of TSV indexes during acute ischemia respect to control situation. Therefore, we could consider the FP as a preferential spatial ECG plane contrasted against HP and SP during LAD occlusion. Shenasa et al. [11], who evaluated the ST-segment shifts in patients undergoing percutaneous transluminal coronary angioplasty stated, for LAD coronary artery occlusion, a significant positive ST-segment shifts on the I, aVL and V1-V6 precordial leads, and significant negative shifts on aVF, II and III leads.

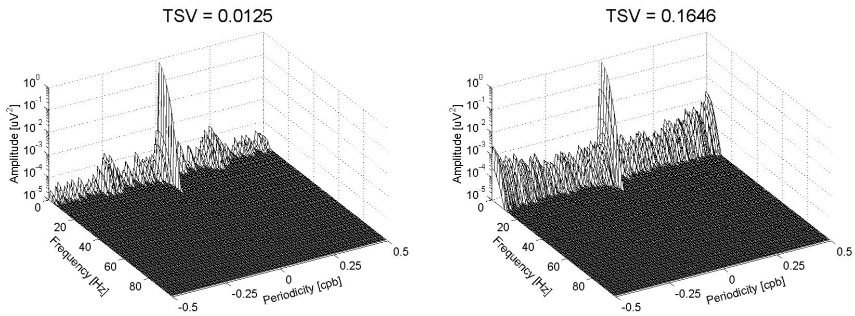
Figure 3b shows that, for LCx occlusion site, both X (it approximately corresponds to I lead, [10]) and Z (it approximately corresponds to v2 lead, [10]) orthogonal leads presented the lowest p-values of TSV indexes during acute ischemia with respect to control situation. Therefore, we could consider the HP as a preferential spatial ECG plane compared to FP and SP during LCx occlusion. Shenasa et al. [11] observed for LCx coronary artery occlusion, a significant positive ST-segment shifts on the III lead, and significant negative shifts on aVL and V1-V3 precordial leads.

Figure 3c shows that, for RCA occlusion site, both Y (it approximately corresponds to aVF lead, [10]) and Z (it approximately corresponds to v2 lead, [10]) orthogonal leads presented the lowest p-values of TSV indexes during acute ischemia respect to control situation. Therefore, we could consider the SP as a preferential spatial ECG plane contrasted against FP and HP during RCA occlusion. Regarding RCA occlusion, Shenasa et al. [11] showed a significant positive ST-segment shifts on the III and aVF lead, and significant negative shifts on I, aVL, V2-V3 precordial leads.

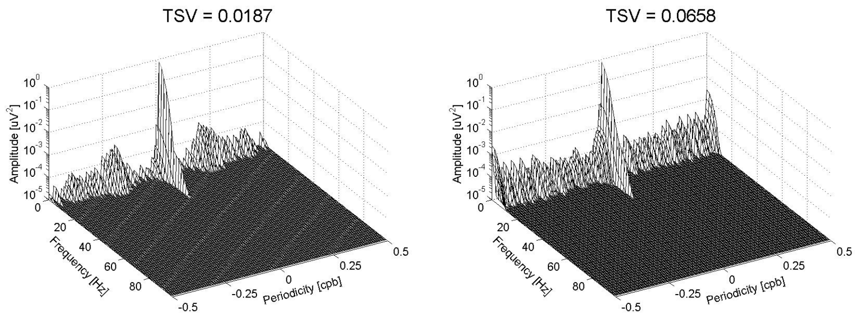
Previously, several studies reported the presence of T-wave alternant (TWA) during PCI procedure, either in ECG surface [16, 17, 18] or in intracoronary ECG



(a)



(b)



(c)

Figure 4: Example of TSV index for three diferent patients in control situation (left) and during PCI procedure (right): (a) lead Y for LAD occlusion site, (b) lead X for LCx occlusion site and (c) lead Z for RCA occlusion site.

[19, 20, 21]. In figure 4 it can be observed a patient with TWA expressed by the presence of an increased power spectrum lobes at $\pm$ 0.5 cpb in right panels with respect to the control situation in the left panels. Also, this example shows an increment of the power spectrum at all the periodicites except to 0 cpb, resulting in a greater TSV index during PCI procedure respect to control situation. TSV index extend the concept of TWA to detect variations at all periodicities and not only at every alternate cardiac beat, that is, a periodicity of $\pm$ 0.5 cpb. Finally, the ischemic regions could act like barriers to the activation and recovering of APD favouring division or fractionation of the wavefronts. This phenomena could produce different patterns of activation and recovery in successive beats, giving a plausible explanation for the beat-to-beat changes in the T-wave, expressed as an increment of the TSV index.

5 CONCLUSIONS

The analysis of the TSV index showed a preferential spatial ECG plane depending on the artery occlusion site. Results showed that the frontal and sagittal planes were coincident with the classical detection of ST-segment shifts during LAD and RCA occlusion sites observed by Shenasa et al. [11]. Conversely, we did not find any relationship between the three spatial ECG planes and the ST-segment shifts for LCx occlusion site. We observed that changes in the TSV index were very dependent on the occluded artery indicating that morphology changes are very dependent on the direction of the equivalent injury current. This can be consequence of the size and location of the artery occluded which in turn generate higher beat-to-beat repolarization variability during acute ischemia. Also, the proposed TSV index could be used in to provided additional information to that supplied conventional parameters to monitoring patients undergoing PCI and/or during ambulatory ECG recordings.

References

[1] J. A. Vassallo, D. M. Cassidy, K. E. Kindwall, F. E. Marchlinski, and M. E. Josephon, "Nonuniform recovery of excitability in the left ventricle," *Circ.*, vol. 78, pp. 1365–1372, 1988.

[2] C. S. Kuo, K. Munakata, P. Reddy, and B. Surawicz, "Characteristics and possible mechanism of ventricular arrhytmia dependent on the dispersion of action potential," *Circ.*, vol. 67, pp. 1356–1367, 1983.

[3] B. Surawicz, "Ventricular fibrillation and dispersion of repolarization," *J. Cardiovasc. Electrophysiol.*, vol. 8, pp. 1009–1012, 1997.

[4] L. Burattini and W. Zareba, "Time-domain analysis of beat-to-beat variability of repolarization morphology in patients with ischemic cardiomyophathy," *J. Electrocardiol.*, vol. 32, pp. 166–172, 1999.

[5] J. P. Couderc, W. Zareba, and L. Burattini, "Beat-to-beat repolarization variability in LQTS patients with the scn5a sodium channel gene mutation," *PACE*, vol. 22, pp. 1581–1592, 1999.

[6] G. Speranza, G. Nollo, F. Ravelli, and R. Antolini, "Beat-to-beat measurement and analysis of the R-T interval in 24hs ECG holter recordings," *Med. Biol. Eng. Comput*, vol. 31, p. 487, 1993.

[7] P. Steinbigler, R. Haberl, K. Nespithal, A. Spiegl, I. Schmücking, and G. Steinbeck, "A new method to determine inhomogeneous repolarization by T wave beat-to-beat variability in patients prone to ventricular arrhythmias," *J. of Electrocardiol.*, vol. 30, pp. 137–144, 1998.

[8] E. R. Valverde, R. A. Quinteiro, P. D. Arini, G. C. Bertrán, and M. O. Biagetti, "Beat-to-beat repolarization variability measured by T wave spectral variance index in chronic infarcted animals," *A.N.E.*, vol. 7, no. 4, pp. 319–325, 2002.

[9] P. Steinbigler, R. Haberl, and G. Steinbeck, "T wave spectral variance for noninvasive identification of patients with idiopathic dilated cardiomyopathy prone to ventricular fibrillation even in the presence of bundle branch block or atrial fibrillation," *PACE*, vol. 27, pp. 156–165, 2004.

[10] A. Pérez Riera, A. Uchida, C. Ferreira Filho, A. Meneghini, C. Ferreira, E. Schapacknik, and S. Dubner, "Significance of vectocardiogram in the cardiological diagnosis of the 21st century," *Clin. Cardiol.*, vol. 30, p. 319:323, 2007.

[11] M. Shenasa, D. Hamel, J. Nasmith, R. Nadeu, J. Dutoy, D. Derome, and S. P., "Body surface potential mapping of ST-segment shifts patients undergoing percutaneous transluminal coronary angioplasty," *J. of Electrocardiol.*, vol. 26, no. 1, pp. 43–51, 1995.

[12] J. Kors, G. van Herpen, A. Sittig, and J. van Bemmel, "Reconstruction of the frank vectorcardiogram from standard electrocardiographic leads: diagnostic comparison of different methods," *Eur. Heart J.*, vol. 11, pp. 1083–1092, 1990.

[13] C. R. Meyer and H. t. Keiser, "Electrocardiogram baseline noise estimation and removal using cubic spline and state-space computation techniques," *Comp. and Biomed. Res.*, vol. 10, pp. 459–470, 1977.

[14] J. Pan and W. Tompkins, "A real-time QRS detection algorithm," *IEEE Trans. on Biomed. Eng.*, vol. 32, no. 3, pp. 230–236, 1985.

[15] J. García, P. Lander, L. Sörnmo, S. Olmos, and P. Wagner, G. Laguna, "Comparative study of local and Karhunen-Loève-based ST-T indexes in recording from human subjects with induced myocardial ischemia," *Computer and Biomedical Research*, vol. 31, pp. 271–292, 1998.

[16] I. Gilchrist, "Prevalence and significance of ST-segment alternans during coronary angioplasty," *The Am. J. of Cardiol.*, vol. 68, no. 15, p. 1534:1535, 1991.

[17] B. Nearing, S. Oesterle, and R. Verrier, "Quantification of ischaemia induced vulnerability by precordial T wave alternans analysis in dog and human," *Cardiovasc. Res.*, vol. 28, p. 1440:1449, 1994.

[18] M. Batur, A. Oto, Z. Ider, S. Aksyek, G. Kabakci, K. vn, L. Tokgzoglu, and F. zmen, "T wave alternans can decrease after coronary revascularization," *Angiology*, vol. 51, no. 8, p. 677:687, 2000.

[19] T. Kwan, A. Feit, H. Chadow, F. Chio, M. Huber, M. Chebacio, S. Breitbart, and R. Stein, "Intracoronary ST-T alternans during coronary balloon angioplasty," *Cath. and Cardiovasc. Diag.*, vol. 35, p. 121:126, 1995.

[20] D. Shah and K. Subramanyan, "Significance of ST alternans during percutaneous transluminal coronary angioplasty," *Indian Heart J.*, vol. 47, no. 3, p. 248:252, 1995.

[21] T. Kwan, A. Feit, M. Alam, E. Afllu, and L. Clark, "ST-T alternans and myocardial ischemia," *Angiology*, vol. 50, no. 3, p. 217:222, 1999.