SENSITIVITY OF T WAVE ALTERNANS DETECTORS TO THE SHAPE OF ALTERNANS TREND

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Abstract: In this article a simulation study of T wave alternans (TWA) is tested in order to compare the performance of TWA detectors for the TWA onset and relaxation measurement. The aim of this article is a comparison of five TWA detectors for the different trends of temporary TWA onset and relaxation. The temporary TWA is not a primary indicator of SCD. It is often important to be aware of temporary TWA in common clinical practice. The TWA onset and relaxation are not fully described yet and they have a variable shape. There is the way to find more detailed description.

Introduction

Microvolt-level electrical T wave alternans (TWA), defined as a consistent 2:l variation in the T wave morphology (Figure 1) has been recognized as a marker of electrical instability in a wide range of experimental and clinical situations, such as congenital long QT syndrome, myocardial ischemia and infarction and several other pathologic conditions. On the other hand [1], TWA is an arrhythmia risk marker to assess subtle changes in repolarization that has been introduced for arrhythmia and Sudden Cardiac Death (SCD) risk stratification.

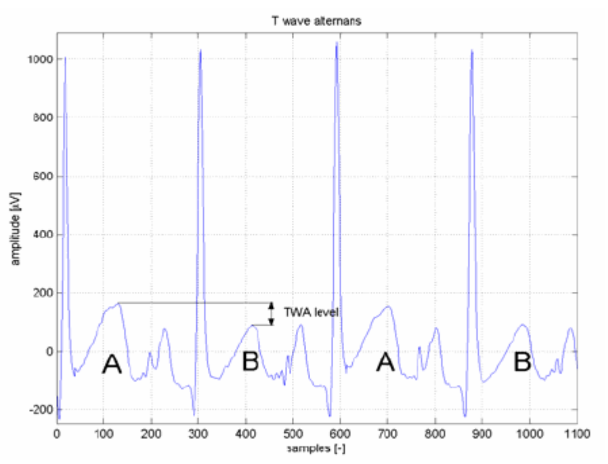

Figure 1 : Introduction of TWA

The TWA trend is a TWA magnitude-time dependence which is associate with the heart rate increment. Briefly, with increasing heart rate, action potential duration shows discordant prolongations in different regions of the myocardium finally resulting in repolarization alternans with opposite phase between neighboring cells. This creates increased spatial dispersion of repolarization associated with undirectional conduction block, reentry and finnaly the occurrence of ventricular fibrilation. On the cellular level, TWA is accompanied by inhomogeneities in the calcium transient indicating that Ca^{++} ions play a key role in the genesis of TWA [2].

Since TWA is heart rate dependent, it's necesary to increase heart rate by either atrial stimulation or noninvasively by drugs or excercise testing for its assessment. Last method contains factors that could interfered with the measurement and also partially affected the TWA trend. They are the patient's respiration rate, the pedaling rate of the ergometer, frequent premature beats , electrodes movement and muscular activity.

The temporary TWA is not a primary indicator of SCD. An example of temporary TWA is shown on the Figure 2 in comparison with sustained TWA. In this case, it was taken the classification criterion from [3]. The occurrence of TWA has not always been sustained.

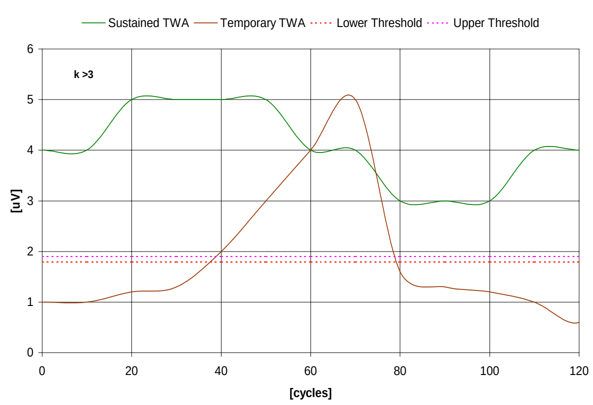

Figure 2 : Comparison of temporary TWA with sustained TWA based on [3].

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It is often important to be aware of temporary TWA in common clinical practice for better decision about the anamnesis. The TWA onset and relaxation are not fully described yet and they have a variable shape. The shape of TWA trends could be problematically evaluated and it could cause the unreal result of TWA detector. In this case, there is no way to find real result. In this article is described the test of sensitivity TWA detectors to the shape of trends of temporary TWA.

Materials and Methods

In this study, the measured data from Department of Internal Medicine and Cardiology, University Hospital Brno were used. The ECG signals had been measured at the heart rate 105 beats per minute with sampling frequency 3000 Hz. The sampling frequency was changed to 500Hz. The resolution is 2.29 μV/LSB. The TWA was simulated by addition or substraction Gauss-window to each second ST-T complex in range from the twentieth to the fortieth beat. The TWA voltage level was chosen 60μV.

Firstly were made preprocessing operations:

ORS detection: FIR-filter based detector was used.

The next step was a suppression of zero baseline fluctuation [7].

Segmentation of the ST-T complex: First step of segmentation was selection of the abnormal beats. The criteria were the amplitude of QRS complex and RR interval. The abnormal beats were replaced by average values from the beats which were not nearest neighbors. The second step was selecting time intervals that were found at a distance from the QRS peak dependent on the RR interval [4]. There were used fourth samples from each T wave.

The following TWA detectors were used in this study:

Spectral Method (SM) - FFT-Based Detector: The TWA magnitude voltage is expressed by performing the Fast Fourier transformation of the beat to beat variation of each sample points over 128 consecutive beats [4]. This number provides a reasonable compromise between the ability to reduce noise and ability to track variations in the TWA level over time. This method is able to identify changes in the T wave occurring at 0.5 relative frequency (cycles per beat). This method does not allow tracking TWA amplitude beat to beat.

Correlation Method (CM): This method compares each consecutive ST-T complex to the median ST-T complex, representative for a series of beats [4]. TWA is detected when the correlation index alternates between values that are grater or smaller than one. If alternating beats are detected in least seven consecutive beats, the TWA episode is detected. It reduces all of the information of the repolarization to only one number whence it follows that is impossible to determine temporal position of TWA within ST-T complex.

Complex Demodulation (CD): To estimate the TWA amplitude each time series is demodulated by multiplying it by a complex exponential function with the desired relative frequency and then the each time series is low-pass filtered [4]. In our case the direct-current component has been removed for better resolution among alternate beats. The main advantages are suitability for analyzing rapidly changing biological signals, tracking TWA amplitude beat to beat and relative insensitivity to phase shifts.

Poincaré Mapping (PM): This method is an alternative to the Fourier Spectrum Method. It is a technique for analyzing dynamic systems displaying its periodic (quasi-periodic) behavior [5]. It is therefore tempting to speculate that fibrillation is a deterministic chaos, especially since definitive evidence of chaos has been found in some simpler cardiac arrhythmias.

Principal Component Analysis (PCA): This method is orthogonal transform [8] techniques that minimize the error between a signal and reduced linear combination of the basis functions [6]. The PCA is computed for every 128-beat set and almost all the energy of signal is concentrated in the first four components. Mainly, the first component has the largest predicative ability about TWA. The presence of the temporary TWA is shown on Figure 4 as an increase contribution of PCA in the range from the twentieth to the sixtieth beat.

The shape of TWA trends: The simulated shape of TWA trends was changed subsequently by ten shape functions. It was chosen eight typical shapes (Sigmoid, Triangular, Generalized Bell, Polynomial, Exponential, Natural Logarithm, Trapezoidal, Unit Pulse) and two non-typical (Uniformly Distributed Random Numbers (UDRN) and White Noise). These last two were used to verify the TWA detectors functionality. The Natural logarithm shape of TWA trend is shown on Figure 4 .

Results

For obtaining of results were used several parameters which are following:

Firstly, it is neccessary to describe the TWA shape in time. It means the TWA onset and relaxation. There are four parameters as is shown on **¡Error! No se encuentra el origen de la referencia.**:

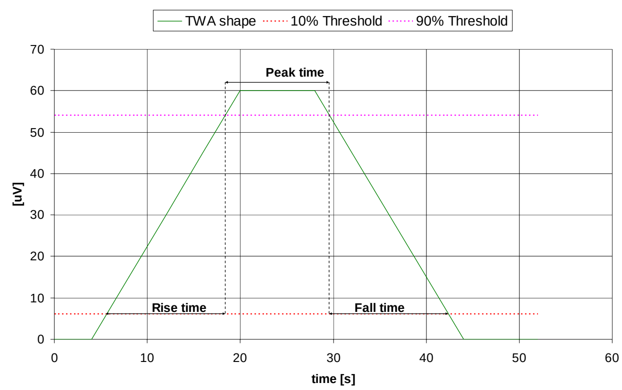

Figure 3 : TWA shape description

1) Type of shape – there were used the shapes described above,

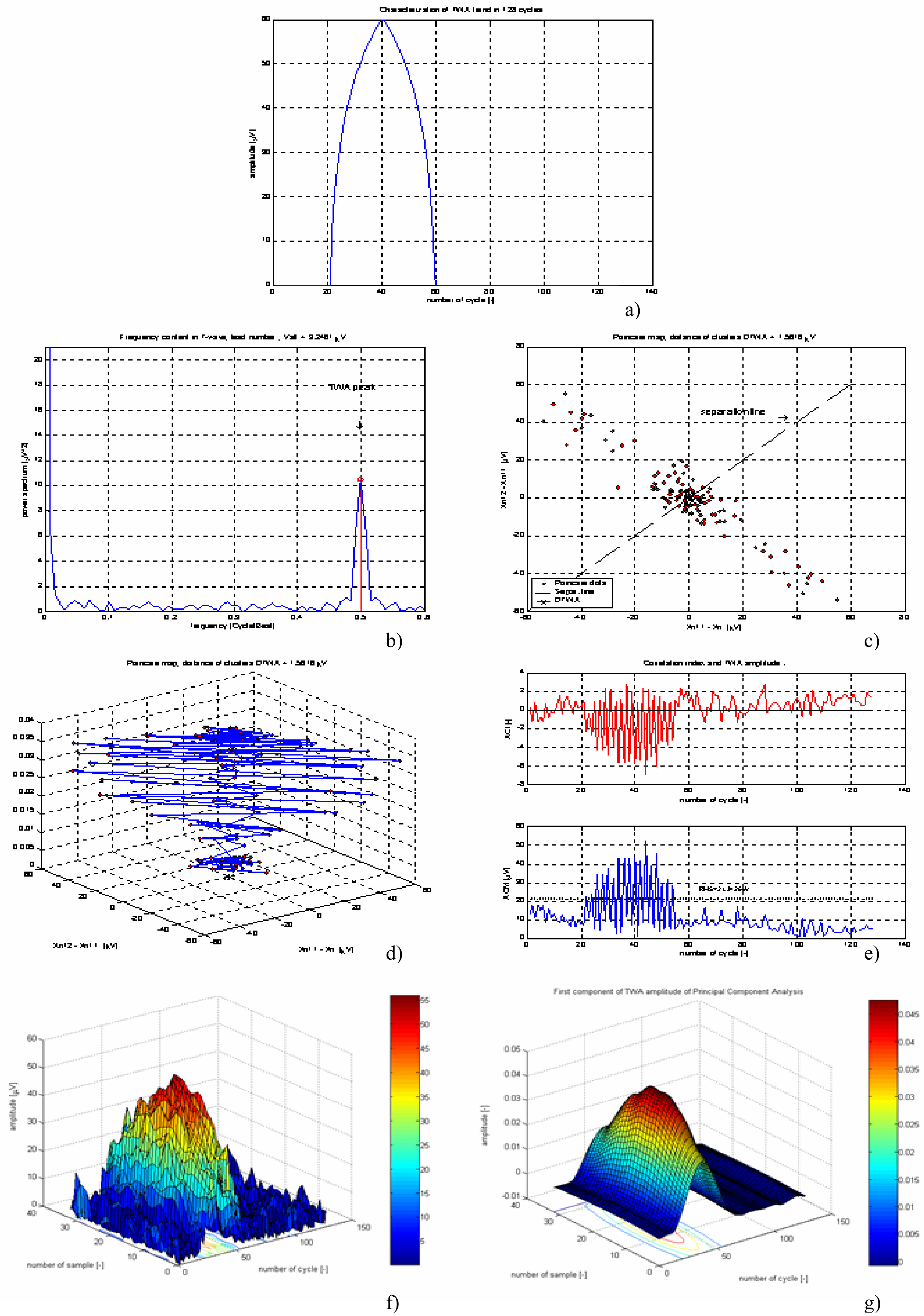

Figure 4 : a) The natural logarithm shape of TWA trend and the results of TWA detectors, b) FFT detector, c) Poincaré Mapping, d) 3D - Poincaré Mapping (z-axis: magnitude of significance distribution density), e) Correlation method detector, f) Complex Demodulation detector, g) PCA detector.

Table 1: Results of the TWA detectors sensitivity test to the shape of alternans trend. r – Pearson correlation coefficient, t - significant test coefficient, C-interval – confidence interval, p – significance of correlation coefficient. For shape 3 and 5 is $p > 0.05$. In other cases is $p < 0.05$.

No.	Input Source			
	Type of Shape	Rise time [s]	Fall time [s]	Peak time [s]
1	Sigmoid	0.92	0.92	16.00
2	Triangular	9.14	9.14	2.29
3	Generalized Bell	1.37	0.46	5.19
4	Polynomial	0.91	0.91	16.23
5	Exponential	1.33	1.33	0.75
6	Natural Logarithm	7.75	7.75	6.51
7	Trapezoidal	2.29	2.29	3.43
8	Unit Pulse	0.40	0.40	21.26
9	UDRN	-	-	-
10	White noise	-	-	-

No.	DSC			Correlation Analysis		
	SM		PM	CD		
	k [-]	Valt [μV]	Description	r	t	C-interval
1	3.77	2.66	3 clusters	0,8129	15,6675	0,7397; 0,8392
2	3,71	2,41	3 clusters	0,8017	15,0555	0,7985; 0,8450
3	3,04	0,79	interspersion	-0,1671	-	-0,4827; 0,1869
4	3,73	2,64	3 clusters	0,9199	26,3312	0,8956; 0.9608
5	5,64	1,32	detectable	0,0615	-	-0,2879; 0,3965
6	3,67	2,61	detectable	0,7764	13,8282	0,7080; 0,8374
7	3,35	2,03	detectable	0,7606	13,1507	0,7188; 0,7956
8	4,12	3,11	3 clusters	0,851	18,1894	0,8010; 0,9012
9	4,21	2,36	interspersion	0,9219	26,7103	0,8988; 0,9627
10	3,45	1,39	interspersion	0,7341	12,1351	0,6828; 0,7731

No.	Correlation Analysis					
	CM			PCA		
	r	t	C-interval	r	t	C-interval
1	0,9427	31,7039	0,9195; 0,9593	0,9267	27,6882	0,8976; 0,9478
2	0,8399	17,3723	0,7801; 0,8845	0,8811	20,9098	0,8352; 0,9147
3	0,1705	-	-0,0031; 0,3342	0,2831	3,3137	0,1153; 0,4353
4	0,9385	30,5032	0,9138; 0,9563	0,9255	27,4189	0,8958; 0,9469
5	0,136	-	-0,0385; 0,3024	0,7686	13,4844	0,6866; 0,8312
6	0,8501	18,1229	0,7937; 0,8921	0,8913	22,0701	0,8492; 0,9222
7	0,858	18,7506	0,8042; 0,8979	0,8821	21,0212	0,8367; 0,9155
8	0,9178	25,9541	0,8853; 0,9414	0,926	27,5364	0,8966; 0,9473
9	0,9014	23,3677	0,8628; 0,9295	0,8983	22,9527	0,8587; 0,9273
10	0,8013	15,0332	0,7291; 0,8558	0,9642	40,8354	0,9496; 0,9747

2) Rise time - the time required for the amplitude of a pulse to increase (rise) from a specified value (usually 10 percent of the peak value) to another specified value (usually 90 percent of the peak value),

3) Fall time - the time required for the amplitude of a pulse to decrease (fall) from a specified value (usually 90 percent of the peak value) to another specified value (usually 10 percent of the peak value),

4) Peak time - the time required for the amplitude of a pulse between rise time and fall time.

The TWA shape numbers three and five have very small energy. It affords opportunity to test the detectors

Secondly, it is important to describe the TWA detectors sensitivity. In this case were used:

1) Correlation Analysis (CA) This parameter is significant for methods which are able to track and copy the TWA shape (CM, CD, PCA). The term correlation means the Pearson correlation coefficient (1), which is a measure of linear association. If two variables tend to move up or down together they are said to be positively correlated. If they tend to move in

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opposite directions, they are said to be negatively correlated. If *r* is 0, *X* and *Y* are said to be uncorrelated. For significance of correlation is necessary to realize the zero hypotheses testing (2) and test for interval of confidence.

$$r = \frac{\sum (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{(x_i - \bar{x})^2 (y_i - \bar{y})^2}} \quad [-] \qquad (1)$$

Where *x* is vector of origin TWA shape and *y* is vector of detector-produced TWA shape.

$$t = \frac{r}{\sqrt{1 - r^2}} \sqrt{n - 2} \quad [-] \qquad (2)$$

Where *t* is the coefficient significant test and *n* is the number beats.

2) Detectable Significant Changes (DSC). This is not unique parameter. It means, there are found all detectable changes in other methods like SM and PM. They are k-ratio and V_{alt} for SM method and visual detectable changes for PM method. In case of PM method, parameter D_{TWA} is not predicative for temporary changes in the TWA shape. For better resolution of temporary TWA is important to take in the account the significance of each of point in Poincaré Mapping. This significance is dependent on magnitude of point distribution density. PM method is more predicative in 3D view. The evaluation of results was made in following scale: interspersion, detectable, 3 clusters.

Conclusions

In this study five methods for temporary TWA detection have been tested. Results of sensitivity test (Table 1) provide that the SM method can't full describe the TWA. There are visible changes of V_{alt} but it is not significant for TWA shape. V_{alt} describe the power of TWA only but it not provide for tracking the TWA shape in time.

On the contrary, it seems that PM method is the good TWA detector, but it is necessary to taking into account the 3D type of the PM presentment. This method is an alternative to the Fourier Spectrum Method but it is more predicative.

The methods CD, CM and PCA were tested for correlation between the vector of origin TWA shape and the detected vector of TWA shape. The Table 1 shows that the best results are linked with PCA detector. We have a strong verification for rejection zero hypotheses in comparison of parameter *t* with tabular values. It is possible to say that the vectors correlate together significantly for each TWA shape. The lower limit of the confidence interval adverts to the strong linear relation. We can say that the PCA detector reflect the origin TWA shape very well. The second possibility of using PCA for TWA detection was the extraction of representative vectors for the ST-T segments. It was not tested.

The CM detector reflects the sigmoid and polynomial TWA shape better than PCA detector. It can not reflect very well the very short temporary TWA.

The CD detector reflects the TWA shape very well. The results are not so good in comparison with the PCA and CM detector.

The TWA onset and relaxation are not fully described yet and they have a variable shape. Finally, it is appropriate in the clinical practice to use the PCA, CM and CD methods for further results.

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