

# Presence of T Wave Alternans in the Statistical Context – A New Approach to Low Amplitude Alternans Measurement

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## Abstract

*Detection of T wave alternans is constructed as a statistical problem in the present work. The objective was to evaluate the performance of a group of statistical tests in detecting a set of artificially generated alternans episodes and in the European ST (EST) database. Three statistical tests- standard t-test, matched pair t-test, and Rayleigh test were performed on numerically generated sequences and also on simulated alternans episodes in a rolling sequence of 32 beats. Application of statistical tests to the numerical simulations and beat simulations resulted in 100% detection accuracy. Statistical tests also detected multiple episodes of both visible and invisible alternans in the EST database. Statistical tests seem to provide a complementary and a computationally efficient solution to alternans detection problem in surface ECG.*

## 1. Introduction

T wave alternans (TWA) is manifested as a variation in T wave segment in every other beat. The variations are possible in sharpness of the peak, peak amplitude, and the morphology of the entire ST and T wave segments. In the present work, the main focus was on reliable detection of the presence or absence of T wave alternans. The present approach makes use of statistical tests, which have been proven to be robust, even under non-normal conditions. The term “robust” is used in the asymptotic sense here, indicating departure from normality. Multiple statistical tests provide increasing power to the decisions made by reducing the uncertainty.

The present work is focused on algorithm development and the results of the algorithm performance on the simulated data sets and with the standard EST database.

## 2. Background

Very low amplitude T wave alternans is invisible in normal strip-chart recordings, but shows consistent presence in every other beat. The improvement in the resolution of the data acquisition systems has dramatically

made possible the measurement of microvolt level changes in ECG signal levels. Current methods to detect and estimate invisible microvolt T wave alternans utilize Fourier transform based estimations for detecting the frequency component at 0.5 cycles/beat [1]. Another approach assumes a similar sinusoidal nature of periodicity and attempts to extract the alternans component by a complex demodulation [2]. Assumption of sinusoidal periodicity leads to several slow-varying noise sources interfering with the estimation of alternating component. Correlation based approaches derive essentially from a spectral approach and they provide a time-domain equivalent to window-based spectral estimation [3].

Detection of alternans is considered a statistical decision making problem in the present context. Computations required for the statistical evaluation of the presence or absence of alternans are performed at every beat, based on a set of 32 previous beats.

### 2.1. Test for difference in means: t-test

This test makes use of the simplest definition of TWA. In the case of alternans, alternate beats seem to show differences in T wave, including the ST segment. The t-test measures the significance of the difference between the ST-T segments of the odd and the even beats. Two groups of data are formed by odd and even beats. For example, group I can be made of the parameter T peak values in odd beats and group II can be made of the parameter T peak values in even beats. Then they can be represented as

$$X_I = \{T_{\text{peak}}(1), T_{\text{peak}}(3), T_{\text{peak}}(5), \dots\} \text{ and}$$

$$X_{II} = \{T_{\text{peak}}(2), T_{\text{peak}}(4), T_{\text{peak}}(6), \dots\}. \text{ Standard t}$$

test is the easiest and the most conventional statistic for measuring the significance of the difference between means of the two groups. The actual value of the t-statistic is calculated as follows:

$$t = \frac{\bar{X}_I - \bar{X}_{II}}{S_D / \sqrt{N}} \text{ where the standard}$$

deviation,  $S_D$ , is calculated as follows:

$$S_D^2 = \frac{\sum_{n \in I} (x_n - \bar{x}_I)^2 + \sum_{n \in II} (x_n - \bar{x}_{II})^2}{N_I + N_{II} - 2} \left( \frac{1}{N_I} + \frac{1}{N_{II}} \right)$$

Here,  $N_I$  = the number of elements in group  $I$  and  $N_{II}$  = the number of elements in group  $II$  [4]. All other parameters like T wave areas and T wave variances can be similarly arranged into two groups. The evaluation of the significance of this  $t$  value with  $N_I+N_{II}-2$  degrees of freedom is done using look-up tables of  $t$  values. For example, for  $N_I=16$  and  $N_{II}=16$ , we get  $t_{30,0.1}=1.6970$ ;  $t_{30,0.05}=2.0420$ ;  $t_{30,0.02}=2.4570$ ;  $t_{30,0.01}=2.7500$ . The fractions 0.1, 0.05, 0.02, and 0.01 indicate the significance value. Here a significance value of 0.01 means that the observed difference has a probability of 0.01 for happening by chance.

## 2.2. Matched pair t-test

In ECG signal recordings, the major slow-moving trend seems to be the respiration-related slow wander with a random phase component. This slow wander is difficult to remove by signal smoothing techniques alone. Matched pair t-test provides the solution in such cases. The assumption in the standard t-test is that the two beat groups are independent. The matched pair t-test, however, assumes that those two groups are dependent and checks for the difference between adjacent beats. The hypothesis-testing problem can thus be considered a one-sample t-test based on the differences ( $d_i$ ).

*Null-hypothesis*  $H_0: d_i = 0$  versus  $H_1: d_i \neq 0$ , when the variance is not known, is based on the mean difference  $\bar{d}$

$$\bar{d} = (d_1 + d_2 + d_3 + \dots + d_n) / n$$

The test procedure is given below. Denote the test statistic  $\bar{d} / (s_D / \sqrt{n})$  by  $t$ , where  $S_D$  is the sample standard deviations of the observed differences:

$$s_D = \sqrt{\left[ \sum_{i=1}^n d_i^2 - \left( \sum_{i=1}^n d_i \right)^2 / n \right] / (n-1)}$$

$n = \text{number of matched pairs}$

For 32 beats,  $n=16$ . The values for matched pair t-statistic is easily found from statistical tables for different values of significance value  $\alpha$ .

## 2.3. Rayleigh test for periodicity

In the case of alternans, the periodicity of interest is of order 2. Rayleigh test is used to test the hypothesis that

the distribution around the unit circle is uniform versus the hypothesis that it follows a random distribution [5].

The Rayleigh parameter  $R$  measures the regularity of the phase reversal present in alternans and compares it with a random beat sequence. The Rayleigh statistic is computed over a length of 32 beats in the present study. This is simply a method to describe if the observed time series follows a periodic pattern or not. The initial step involves the generation of a statistic based on simulations. A random sequence of 32 numbers satisfying a symmetrical, leptocurtic pattern in normal distribution is generated. The choice of the distribution is based on the study of T wave parameters from ECG records in three standard ECG databases [6]. The number of deviations from ideal alternans behavior is calculated for the sequence. This is repeated multiple times to arrive at the probability that this occurrence is possible by noise or a set of random numbers.

A table of Rayleigh measures based on observations of 1,000,000 iterations of randomly generated sequences of length=32, provides the probability values in Table 1. These values indicate the chance of alternans happening in a random sequence of 32 beats. Alternans is defined here in terms of either [ABAB....] or [BABA....] patterns, a two-way probability measure. A scoring system is again used to indicate the presence of alternans, based on the number of times the observed time series deviates from the alternans pattern.

For example, if a series of T wave peak values from 32 consecutive beats show a pattern such that  $\{T_{\text{peak}}(1) > T_{\text{peak}}(2), T_{\text{peak}}(2) < T_{\text{peak}}(3), T_{\text{peak}}(3) > T_{\text{peak}}(4), T_{\text{peak}}(4) < T_{\text{peak}}(5), \dots\}$  for 32 beats without a single deviation, then the score for the presence of alternans is  $(1-\text{chance}) * 100 = 100\%$ , based on the Table 1 for deviations=0. If the pattern deviates 7 times out of 32 beats, then the score for the presence of alternans is reduced to  $(1-\text{chance}) * 100 = 99.875\%$  and so on. Other T wave parameters can be tested similarly. Correlation with other parameters is the simplest approach to validate the Rayleigh test. The Rayleigh test is specifically tuned for the problem of alternans detection in the present study.

## 3. Implementation

Simulation studies are needed to verify the performance of the statistical tests due to the very low amplitude level of the T wave alternans being measured. In the present study, the performance of statistical tests was evaluated for several simulated patterns.

Table 1 Rayleigh Test – Significance values for different number of deviations from ideal alternans pattern in 32 beats

Deviations	0	1	2	3	4	5	6	7	8	9	10	11
Chance	0	0	0	0	0	0.00003	0.00040	0.00125	0.00450	0.01250	0.02940	0.06000

### 3.1. Simulation with numerical patterns

Patterns are the simplest approach to start the simulation process. Initial assumption is that T wave parameters are available for 64 beats and they are devoid of any errors in calculation. The initial 32 beats are used for initializing the parameters. Noise-free alternans pattern is added with various noise patterns to mimic real situations. Noise stress test is performed with increasing noise-to-signal ratio (NSR) levels. Phase reversal had only a momentary false negative due to the small window of 32 beats used in statistical tests. The results are presented in Table 2.

Table 2. Results of Statistical Tests with Numerical Simulation for Alternans

Tests	t-test	Matched pair t-test	Rayleigh test
Simulations $Xn=[1\ 2\ 1\ 2\ 1\ 2\ \dots]$	**	**	**
$Yn=Xn+Nn$ ( $Nn=noise$ )	*	*	*
$Yn=Xn*Rn$ ( <i>Slow wander</i> )	#	#	#
$Yn=aXn+b$ ( <i>Linear trend</i> )	**	**	**
$Yn=Xn+Xn'$ ( <i>Phase reversal</i> )	0*	0*	0*

\*\* - Pr < 0.0001 0\* - False negative is momentary

\* - Pr<0.001@NSR=0.7777 dB (NSR=1.2)

# - Pr<0.0001@NSR=0 dB (NSR=1)

### 3.2. Simulation with ECG database

The objective of simulation of alternans pattern in simulated identical beat sequences is to evaluate the performance of statistical tests in detecting the hidden alternans episodes in a ECG signal. Here, a single beat is chosen from lead 0 of record e0103a from the EST database. This clean beat is periodically re-generated and small hulls are added around the T wave peaks to create episodes of alternans at different time intervals. Hulls were added to alternate beats to simulate an alternans pattern. Hulls were generated using the Kaiser and the triangular window functions. The middle point of an eleven-point hull is made to coincide with T wave peak. Hulls were also skewed to shift the T wave peaks in alternate beats to simulate another case of alternans. The algorithm detects the R fiducial point and the T fiducial point and adds the hull repeatedly in selected segments. Episodes lasted between 20 to 80 seconds.

In each beat, computed T wave parameters included T wave peak ( $T_{peak}$ ), T wave area around the peak ( $T_{peakarea}$ ), and variances of four T wave segments at fixed intervals from R fiducial point ( $T_{var1}$ - $T_{var4}$ ). Computations for the T wave parameters are given below.

$$T_{peak} = \max \{T(i)\}_{T_{start}}^{T_{end}} \quad T_{peakarea} = \sum_{i=T_1}^{T_2} T(i)$$

$$T_{var} = \frac{\sum_{i=1}^n (T(i) - mean)^2}{(n-1)}$$

$T_{peakarea}$  is calculated for 67 milliseconds ( $T_2-T_1$ ) around the  $T_{peak}$ . Parameters  $T_{var1}$ ,  $T_{var2}$ ,  $T_{var3}$ ,  $T_{var4}$  are all calculated using the formula for  $T_{var}$ . The values of variances are calculated for T wave segments at (62.5-125) milliseconds, (125-187.5) milliseconds, (187.5-250) milliseconds, (250-312.50) milliseconds from R fiducial point. The sampling rate ( $F_s$ ) chosen for the present study was 256 Hz and the values of  $T_1$ ,  $T_2$  and  $n$  were based on  $F_s$ . The above parameters hold true for heart rates between 55 and 120 beats per minute and only  $T_{var4}$  may become unreliable at the higher heart rates.

At any time, T wave parameters from a rolling window of 32 beats were utilized to detect the presence of alternans. All three statistical parameters were sensitive to the presence of alternans and the detection sensitivity and specificity were 100%. No alternans was detected when the simulation was not performed (100% specificity).

In addition to the above simulations, a noise pattern was added to and around the hull in the T wave. Noise power varied randomly between 10-118% of signal power depending on the shape of the hull pattern. Sensitivity and specificity of statistical tests were not affected even at an NSR=0 dB. Figure 1 illustrates the mean performance of the statistical parameters with increasing noise in multiple simulations.

### 3.3. European ST-T database studies

The European ST-T database provides two lead ECG recordings with annotations for the verification and validation of ECG repolarization measurements. Annotations are available for ST and T wave changes and signal quality. Studies utilizing complex demodulation techniques in EST database detected several episodes of T wave alternans [7]. In the present work, the database study followed the same approach as performed on the simulated ECG beats in section 3.2. Use of variance parameters overcame the effects of any possible errors in T wave fiducial point detection. Variance parameters made use of ST-T segments fixed distance from R fiducial points and are unaffected by errors in T wave fiducial point. Errors in T wave identification are readily identifiable by abnormal variations in beat-to-beat RT interval measurements. T wave parameters from the previous 32 beats were utilized for the T wave alternans detection as explained in section 3.2.

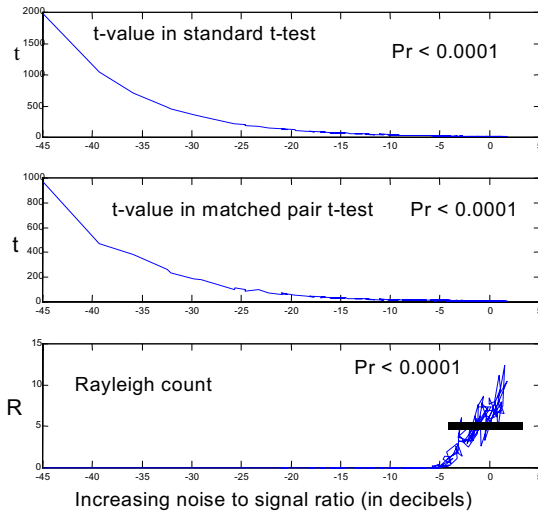


Figure 1. Performance of statistical tests in detecting alternans in the presence of increasing noise

Analysis was performed on both leads in the database independently and many episodes were present in only one lead. Alternans is considered present when one of the statistical parameters show the presence with more than 99.5% significance. Each episode was checked manually for the absence of T wave detection errors or ectopic beats. All chosen episodes indicated strong presence of alternans according to more than one statistical test. A detected sample episode is given in Figure 2. The episode lasted for around two minutes (26:00-28:00) in the record e0139a. Mean odd and mean even ST-T segments are plotted from 164 beats in that time frame. Such a representation is possible at each beat regarding the previous 32 beats. In the present study, actual calculations were performed at every beat and the alternans amplitude varied widely inside this two-minute window. All three statistical parameters were sensitive in this time window and they also showed variations with varying alternans magnitude and with different T wave parameters.

#### 4. Discussions and conclusions

In the present study, statistical tests provide a measure of alternans along with a significance value regarding the measure. Different types of noise may affect one of the three chosen statistics; however, it is anticipated that the diagnostic power of the three tests taken together will not be adversely affected by false-positives. There were TWA episodes in the EST database where the statistical tests were less sensitive compared to Periodicity Transform [8].

Parametric statistical tests alone may not be sufficient indicators of alternans since the T wave parameters show deviations from ideal normality behavior in many

instances. However, they can provide increased accuracy, when used in combination with non-parametric tests or signal-processing techniques such as Periodicity Transform [8].

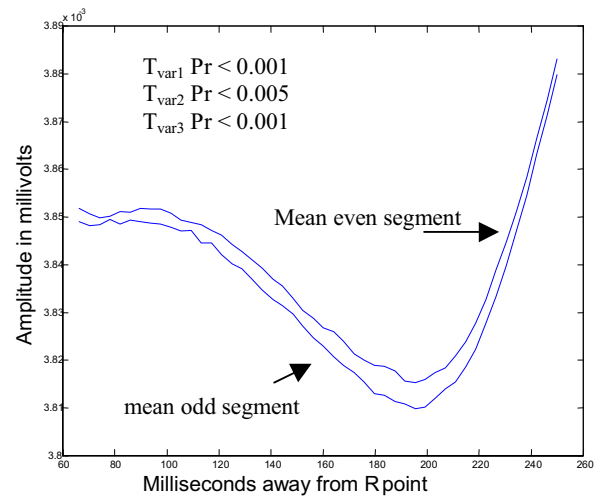


Figure 2. Mean odd and mean even ST-T segment plotted for a two minute window in record e0139 of EST database

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