

Predicting Imminent Episodes of Ventricular Tachyarrhythmia using Heart Rate

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ABSTRACT

Background: A reliable predictor of an imminent episode of ventricular tachyarrhythmia that could be incorporated in an implantable defibrillator capable of preventive therapy would have important clinical utility.

5 *Method:* A test set of 208 R-R records saved by defibrillators spanning a mean of 1.6 hours before sustained tachyarrhythmia were used to derive criteria that would improve the specificity of the previously identified monotonic heart rate acceleration predictor. Additional criteria were used, namely two such patterns need to occur within a period of 1.8 hour and the heart rate during these accelerations exceeds 86 bpm (700 ms). The specificity was tested using R-R
10 records matched in duration from 26 control patients with defibrillators during normal periods.

Results: The basic acceleration pattern was found during sinus rhythm in the 1.8 hour period prior to 83% of episodes of ventricular tachyarrhythmia. It was also found in 43% of the matched set of non-arrhythmic records, corresponding to a specificity of 57%. With the two extra
15 requirement of multiplicity within 1.8 hour and peak heart rate, the sensitivity of the proposed predictor is reduced to 53%, but the specificity is increased to 91%, which corresponds to an average false positive rate of 0.8 event/day across the patient population.

Conclusion: A ventricular tachyarrhythmia predictor based on a pattern of heart rate acceleration has been proposed that can yield sensitivity from 53% to 69%, with specificity up to 91%. Instances of this predictor increase significantly prior to an episode of tachyarrhythmia.
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Keywords: prediction, ventricular tachyarrhythmia, R-R intervals, ICD, prevention, VT, VF.

1. Background

25 A reliable predictor of an imminent episode of ventricular tachyarrhythmia (VTA), namely ventricular tachycardia (VT) or ventricular fibrillation (VF), could have important clinical utility (1) that might include incorporation into an implantable cardioverter defibrillator (ICD) that would be capable of delivering preventive therapy. Prediction of impending episodes of VF was investigated by Skinner, et al. (2). They proposed the correlation dimension PD2 of R-R intervals
30 as a predictor of VF (sensitivity: 91%; specificity: 85%). Though an excellent result, this was a limited study including only 38 patients (11 with VF, 14 with nonsustained VT, 13 with premature ventricular complexes) and employs a computational complex algorithm that is not suitable for an ICD with limited power resources. Mäkikallio et al. (3) using similar non-linear methods found statistically significant reductions prior to the onset of VTAs in the short-term
35 correlation exponent α of R-R intervals and the power-law slope β . This was also a limited study with an analysis of the Holter records of 15 patients who had experienced an episode of VF or VT during recording, namely 8 with VF, 3 with fast monomorphic VT, 4 with polymorphic VT degenerating into VF. They were matched to 30 postinfarct patients without a history of ventricular tachyarrhythmia. This method is more suitable for retrospective analysis
40 than for prediction, since it requires large amount of data past and future. Recently the research on VTA predictor has shifted towards heart rate variability (HRV) (4) using heart rate data collected from Holter recordings (5 - 7) and intracardiac rate measurement from ICDs (8 -11). While certain properties in the heart rate variability were found, no VTA predictor was explicitly suggested. Thong et al. (12, 13) have recently described a simple predictor based on a
45 beat by beat heart rate analysis. A particular pattern or heart rate acceleration was found to occur

frequently before an episode of VTA. In this paper we present a modified version of this predictor along with clinical results.

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2. Methods

2.1. Databases

A set of 208 R-R interval records from 90 subjects was selected from the Biotronik® (Berlin, Germany) European HRV database. These are R-R records stored by Biotronik® Phylax™ XM and mycro Phylax™ single chamber implantable ICDs, prior to device detected episodes of VTA. The records were obtained from European patients between 1997 to 2000. R-R records used in this study were selected according to the following criteria:

- At least 600 R-R interval long
- No visible indication of pacing in the record
- No visible indication of supraventricular tachyarrhythmia in the record.

This dataset will be referred to as the Bio-ICD database. Complete demographic data was not available for all the Bio-ICD patients. An example tachogram from this database is shown in Figure 1. The distribution of the record lengths is shown in Figure 2. A specific R-R acceleration pattern (12) was identified by examining a development set of 39 Bio-ICD records recorded before episodes of VF. The sensitivity of the predictor was tested in the remaining 169 records that were recorded before episodes of either VT or VF.

2.2. Algorithm Development

Interpolating all premature events with compensating intervals, and ignoring isolated premature intervals, acceleration patterns which are consistently faster than a long term average of the heart rate are monitored (12). The acceleration pattern is terminated when the heart rate becomes equal or slower than the long term average. We started with an acceleration pattern with a duration of 50 R-R intervals as VTA predictor (12). To improve specificity, we added a dual acceleration requirement (13). To further improve specificity, we investigated the following additional criteria: the peak heart rate during acceleration, the difference in heart rate between the beginning and the end of the acceleration, the slope of the acceleration. Of these 3 additional criteria, only the peak heart rate was effective in improving specificity. But, as is the case with any additional criterion, the sensitivity suffered. This led us to decrease the duration to 40 R-R intervals which improved sensitivity, while keeping the false positive rate at less than 1 event per day.

The algorithm to predict an imminent episode of VTA thus consists of

1. Detection of a mostly monotonous rate acceleration pattern during sinus rhythm (12). An example of such an acceleration pattern occurs at -600 seconds in Figure 1.
2. This acceleration pattern must last in excess of 40 R-R intervals to qualify.
3. Two such acceleration patterns must occur within 1.8 hour
4. The heart rate must exceed 86 bpm (700 ms) during at least one of these acceleration patterns.

The simple acceleration predictor consists of using just criteria 1 and 2. In (12), a pattern length of 50 R-R intervals was used. More advanced predictors are achieved by adding criterion 3 and/or criterion 4. In (13) criteria 1, 2 and 3 were used with acceleration lengths of 50 and 65

R-R intervals. The new VTA prediction pattern (VTAPP) is defined as an acceleration that meets all four criteria.

The sensitivity of the predictor is defined as the percent of records in the Bio-ICD database in which the acceleration pattern occurred. The variable lengths of the R-R records make this measure of sensitivity somewhat inaccurate. To obtain a better estimate of sensitivity, a Kaplan-Meier survival analysis (14) was performed. For each record, starting backward from the onset of the VTA, we define the end point to be either the beginning of the record (drop out) or the time at which the criteria to be tested are met.

In the Bio-ICD database, multiple records are available for a number of subjects. For each of these subjects, we computed the probability of prediction success. The average over this subset of subjects is then compared to the sensitivity figures for the complementary subset, which consists of records from subjects with a single record to assess the impact of using multiple records from a common subject.

To assess the specificity of the acceleration pattern 24 hour Holter monitor (Model 90208, Burdick Spacelabs, Deerfield, Wisconsin, USA) recordings were made in 28 volunteers who had ICDs. This study was approved by the Institutional Review Board of Portland (Oregon) Veterans Affairs Medical Center and patients provided written informed consent to participate. Two of the initial records were lost due to faulty setup of the Holter monitors. Thus, only 26 records were available for analysis. The R-R interval history was automatically extracted from the Holter tape using software from the Holter monitor manufacturer. This dataset of R-R history will be referred to as the VA-ICD database. No episode of ventricular tachyarrhythmia was recorded in these records. Thus, any occurrence of the predictor in these recordings, could be considered a false positive. For each record in the Bio-ICD database, one of the 26 records in the VA-ICD database was chosen at random together with a random starting time, and a record with the same length as the one from the Bio-ICD database was created. The resulting database will be referred to as the surrogate-VA-ICD database. The specificity of the acceleration criteria were defined as 1 minus the percent of false positive detected in the surrogate-VA-ICD database with the appropriate prediction criteria. Since the average record length is 1.6 hours, the rate of false positive in the surrogate-VA-ICD database can be considered to be representative of the average false positive rate in 1.6 hours. Since prediction is an on-going process, the daily rate computed directly from the average rate of false positives in the 24 hour Holter records is a more convenient measure, and this avoids the use of the surrogate database. Furthermore since we use 1.8 hour between accelerations to confirm the prediction, we define an episode of acceleration as a string of acceleration patterns with each pattern occurring within 1.8 hours from the previous pattern in the string. Each such string in the VA-ICD database counts as one false positive.

2.3 Tools

All the software programs used in the analyses presented in this report were developed in MATLAB, The MathWorks, Inc., Natick, Massachusetts. Statistical evaluation was performed using Microsoft Excel.

3. Results

Table 1 shows the profile of the patients who contributed data to the Bio-ICD and VA-ICD databases.

The sensitivity of the acceleration pattern (criteria 1 and 2 in Section 2.2) as a predictor of VTA is reported on the first data line in Table 2. The Bio-ICD database in the first two data columns is split into the “development” subset and the remaining subset. The basic acceleration predictor was developed using the “development” subset and verified on the other subset. Another split is into the subset of subjects (46 out of 90) with multiple records and those with single records. In the “All” column, all the records are treated as independent. The Kaplan-Meier curve in Figure 3 was used to correct for the effect of the variable record length. Had all the records been 2 hours long, 83% of the VTAs would have been predicted. The surrogate-VA-ICD is used to evaluate the specificity. The false positive rate shown has been Kaplan-Meier corrected. In the remaining lines of Table 2 the performances of the progressively more specific predictors are summarized. The Kaplan-Meier curves for the acceleration patterns with a peak heart rate greater than 86 bpm are shown in Figure 4. The Kaplan-Meier curves for the full VTAPP are shown in Figure 5.

If instead of computing the specificity using the surrogate-VA-ICD database, the daily (24 hour) false alarm rate is computed directly from the VA-ICD database, we obtain the VTAPP results presented in Table 3.

Figure 6 shows that monotonic accelerations were more likely to occur just prior to episodes of VTA than earlier in the monitoring period, and definitely at a higher rate than in random records of ICD patients.

The peak heart rate can also be used to fine-tune the VTAPP by trading off sensitivity for false alarm rate, as shown by the receiver operating curve of Figure 7.

4. Discussion

4.1 Predictor acceleration patterns

We have shown that a monotonic heart rate acceleration is common (83%) in the 1.8 hours before an episode of VTA but is less frequently seen (43%) in randomly selected time matched segments from ICD patients not preceding an episode of VTA. One such acceleration can be observed in the time interval from -600 seconds to -500 seconds in Figure 1. This is an unusual acceleration, due to its duration and its monotonicity. The monotonicity of this acceleration is apparent when compared to the more typical acceleration starting around -1500. Thus, a pattern of prolonged, slow and mostly monotonous acceleration during sinus rhythm has been used as a predictor of imminent VTA. The predictor pattern is considered to be valid when the duration of the mostly monotonous acceleration exceeds a programmed length, measured in the number of R-R intervals. For the results presented in this report, the minimum duration used was 40 R-R intervals (~30 seconds). The acceleration at -600 seconds in Figure 1 is an extreme example of this type of acceleration, being over 170 R-R intervals long and lasting 116 seconds.

It is interesting to note that monotonic accelerations were observed more frequently in the test set of the Bio-ICD database than in the development set, as reported in Table 2. This may be a result of the fact that the development dataset was exclusively made up of intervals before episodes of VF while the test dataset included R-R intervals records associated with VT and VF episodes. The difference when a double acceleration criteria is added is significant. A possible explanation could be that a VF develops faster than a VT, thus there is less time for a second acceleration to occur.

The differences between the sets of records from subjects with multiple records and those with single records in the Bio-ICD database are small. There is only a difference of at most 5%

between the data in the third and fourth columns of Table 2. Since the number of records for a particular subject is related to the frequency of VTA episodes, this appears to imply that a subject history of VTA does not affect the performance of the predictor.

5 If there were a link between the VTA and the acceleration we would expect that as the VTA becomes more imminent, there would be an increase in the rate of acceleration patterns. This is confirmed in Figure 6 where it can be seen that the majority of episodes of monotonic acceleration occur in the 20 minutes prior to an episode of VTA. The higher frequency of these accelerations in patients prior to an episode of VTA compared to that seen in the control population and the clustering of the accelerations in the few minutes before episode of VTA
10 suggests these accelerations may be a clue to an autonomic trigger of VTA.

The false alarm rate of 9% for VTAPP presented in Table 2 can be viewed as an estimate of the false alarm rate for 1.8 hours following the Kaplan-Meier correction for non-uniform record length. The corresponding 24 hour rate would be 1.2 event per day. This is higher than the 0.79 event per day reported in Table 3. The reduction comes from the merging of the false
15 positives which occur within 1.8 hour from each other.

4.2 Speculation about the underlying mechanism of the accelerations

Without definite proof, we can only speculate that in addition to the conventional hypothesis of VTA genesis by an arrhythmogenic substrate and a trigger (15), a particular
20 autonomic substrate is also required just prior to a VTA. Our speculation is that this is a temporary vagal fatigue, in addition to the chronic vagal depression (16) and increased sympathetic activity seen in patients with severe heart disease. A clue is that, prior to a VTA, the acceleration patterns, which are likely to be associated with increased sympathetic surges, terminate at a higher heart rate. In Figure 3 we find that an acceleration pattern can be found in
25 40.4% of the records within 12 minutes (0.2 hour) of the end of the record, and in 83.3% of the records within 2 hours. In Figure 4, requiring an acceleration to at least 86 bpm, the corresponding percentages are 35.6% and 69.4%. Thus in the last 12 minutes prior to a VTA, 88% of the accelerations meet the 86 bpm rate requirement. In the 2 hours prior to the VTA, but excluding the last 12 minutes, 71% of the accelerations meet this heart rate requirement. By
30 comparison, using the surrogate VA-ICD database, only 36% to 41% of the accelerations meet the rate requirement when there is no associated VTA. A possible explanation for this observation could be that the vagal system, which would normally intervene to terminate the acceleration, does not become energized until the acceleration becomes critical, i.e. the heart rate is much higher than optimal. Furthermore, the vagal intervention to stop the accelerations occurs
35 at higher heart rates as the VTA becomes imminent.

4.3 Comparison with previous studies

The presence of these acceleration patterns, reduces the randomness and chaos of the heart rhythm. This may explain the earlier findings by Skinner et al. (2) and Mäkikallio et al. (3).
40 The interesting finding of Skinner is that the reduction occurs hours before the VTA. Since our average record length is only 1.6 hour, we are not able to verify this. Could it be that the rate of acceleration patterns, defined as the average over a sliding window of 10 minutes, starts increasing hours before, but still remain at a low level, until the last 2 hours, in agreement with Figure 6? In Figure 6 this rate, just prior to the VTA, is ten times higher than in the 2 hours prior.

45 The findings by Shusterman et al. (5, 6) of a decrease in the HRV low-frequency (17) power, in the range from 40 mHz to 150 mHz, as the heart rate is increased prior to the VTA

could also be explained by the presence of the acceleration pattern. When such acceleration takes place, the power is shifted towards the very low frequency band, defined to be from 3 mHz to 40 mHz. While the high frequency power, from 150 mHz to 400 mHz could be unchanged, there is a significant reduction in the low frequency power in the 40 – 150 mHz band.

5 The other finding by Shusterman et al. (6) that most of the changes in HRV appear to be confined to the 15 minutes prior to onset of the VTA, and that almost all the changes are confined to 2 hours is consistent with our findings. In Figures 3 and 4 the distribution of the last acceleration pattern prior to the VTA is shown. The non-linear behavior of the curve is an indication that the last acceleration pattern prior to the VTA is not uniformly distributed. Thus, when mean and power measurements are averaged over any large dataset, the average effect of the acceleration patterns will be small, and may not reach statistical significance. This may be the reason that these acceleration patterns were not detected in prior analyses (7-11) with conventional measures.

10 Pruvot et al. (8) investigated the linear detrending used in the conventional analysis. They observed that R-R signals before VTA contain a nonlinear increase whose power is concentrated in the very low frequency band. This is consistent with the presence of acceleration patterns.

15 Meyerfeldt et al. (10) investigated unconventional nonlinear measures and reported an increase in short phases with low variability (successive segments of R-R with less than 10 ms difference). This could be explained by the slow acceleration patterns with R-R values changing very slowly.

20 In the three previous studies that used stored ICD R-R interval histories (8-10), the acceleration pattern discussed in this paper can be observed in at least one of the VTA tachograms displayed.

25 **4.4 Treatment of ectopic beats**

 In the evaluation of the VTAPP, premature events, both of ventricular and atrial origins, are interpolated, i.e. replaced by two intervals that are the average of the premature interval and the following compensating interval, since the predictor operates on the medium term trend of the heart rate. As a result, VTAPP, while physiologically based on a fluctuation of the sinus rhythm, is not related to the premature ventricular contraction based heart rate turbulence dynamics (18), which uses a five R-R interval slope deceleration measured off averaged heart rate data. VTAPP uses the real-time heart rate and is a longer trend, namely longer than 40 R-R intervals.

35 **4.5 Clinical implications**

 The ability to predict imminent episodes of VTA produces the opportunity to prevent them. Unlike the more complex heart rate variability measures described above, detection of monotonic accelerations is not a processor intensive process and could be easily incorporated into an ICD. Such an ICD might be programmed to perform transient overdrive pacing or other preventive maneuvers such as antiarrhythmic infusion if one of the monotonic acceleration criteria were met. Though episodes of monotonic accelerations are most likely to occur prior to an episode of VTA we have shown that they also occur with a low frequency in patients at high risk for VTA (ICD patients). Whether the occurrence of monotonic accelerations during Holter monitoring might have prognostic value for determining the future risk of VTA remains to be determined.

4.6 Limitations of current study

The main limitation of the current study is the fact that heterogeneous data are used. The subjects in the sensitivity study are not the same used in the specificity study. The differences in the two populations, as detailed in Table 1 may reflect changes in indication from 2000 to 2004. In general, based on age, CAD and MI histories, the control population appears to have more severe heart disease.

The original work that uses the acceleration pattern was developed using only 39 records of the Bio-ICD database, as indicated in Table 2. The sensitivity and specificity were then verified using the other records. Thus, the results on the first line of Table 2 follow the strict rule of separation of development and test data. When additional criteria were developed, the decision whether to use them or not was based on the performance achieved with the whole set of data. As a result, the results presented here should be validated against new data.

The study of the control group was limited to 24 hours. The results in Table 3 indicate that a large number of subjects, namely 15 out of 26, exhibit no VTAPP. A longer duration study would be needed to answer the question whether this is a snapshot effect or part of this subgroup experiences a very low rate of false positive. In the latter case, this subgroup would be an ideal target for the VTAPP.

Another limitation of this study is that only subjects in sinus rhythm were considered. Records with visible pacing or supraventricular artifacts, in particular unstable ventricular rate typically associated with atrial fibrillation, were not selected to be included in the Bio-ICD database. This selection bias could have affected our results.

5. Conclusion

In this paper we have presented a predictor of an imminent episode of VTA. To the basic predictor, which can achieve a sensitivity of 83%, we can add two additional criteria, namely a peak acceleration of at least 86 bpm, and a dual acceleration pattern requirement, to improve the daily average false positive rate down to 0.8 event/day. Including all criteria, reduces the sensitivity to 53%. In any particular patient, it may be possible to turn on just one (most likely the peak rate of 86 bpm requirement) or both additional criteria, for achieving sensitivity in the range from 53% to 69%, depending on the patient's pattern of false positive and the potential severity of adverse effects as a consequences of inappropriate preventive therapy delivery.

Other observations from this study are:

- The predictor appears to be more effective at predicting episodes of VT than episodes of VF.
- The subject history of past VTA episodes does not appear to affect the performance of the predictor.
- Instances of the predictor increase prior to an episode of VTA.

The last two observations appear to indicate that the VTAPP is just a function of how imminent the VTA is.

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References

1. Rubart M, Zipes DP: Mechanism of sudden cardiac death. *J Clin Invest* 2005; 115: 2305-2315.
- 5 2. Skinner JE, Pratt CM, Vybiral T: A reduction in the correlation dimension of heartbeat intervals preceded imminent ventricular fibrillation in human subjects. *Am Heart J* 1993; 125: 731-743.
3. Mäkikallio TH, Koistinen J, Jordaens L, Tulppo MP, Wood N, Golosarsky B, Peng CK, et al.: Heart rate dynamics before spontaneous onset of ventricular fibrillation in patients with
10 healed myocardial infarcts. *Am J Cardiol* 1999; 83: 880–884.
4. Reed MJ, Robertson CE, Addison PS: Heart rate variability measurements and the prediction of ventricular tachyarrhythmias. *QJM* 2005; 98: 87-95.
5. Shusterman A, Aysin B, Gottipaty V, Weiss R, Brode S, Schwartzman D, Anderson KP: Autonomic nervous system activity and the spontaneous initiation of ventricular tachycardia.
15 *J Am Coll Cardiol* 1998; 32: 1891-1899.
6. Shusterman V, Aysin B, Weiss R, Brode S, Gottipaty V, Schwartzman D, Anderson KP: Dynamics of low-frequency RR interval oscillations preceding spontaneous ventricular tachycardia. *Am Heart J* 2000; 139: 126-133.
7. Zimmerman M: Sympathovagal balance prior to onset of repetitive monomorphic idiopathic
20 ventricular tachycardia. *Pacing Clin Electrophysiol* 2005; 28: S163-167.
8. Pruvot E, Thonet G, Vesin JM, Van-Melle G, Seidl K, Schmidinger H, Brachman J, et al.: Heart rate dynamics at the onset of ventricular tachyarrhythmias as retrieved from implantable cardioverter-defibrillators in patients with coronary artery disease. *Circulation* 2000; 101: 2398-2404.
- 25 9. Lombardi F, Porta A, Marzegalli M, Favale S, Santini M, Vincenti A, DeRosa A: Heart rate variability patterns before ventricular tachycardia onset in patients with an implantable cardioverter defibrillator. *Am J Cardiol* 2000; 86: 959–963.
10. Meyerfeldt U, Wessel N, Schütt H, Selbig D, Schumann A, Voss A, Kurths J, et al.: Heart rate variability before the onset of ventricular tachycardia: differences between slow and fast
30 arrhythmias. *Int J Cardiol* 2002; 84: 141-151.
11. Burri H, Chevalier P, Arzi M, Rubel P, Kirkorian G, Touboul P: Wavelet transform for analysis of heart rate variability preceding ventricular arrhythmias in patients with ischemic heart disease. *Int J Cardiol* 2006; 109: 101-107.
12. Thong T, Goldstein B: Prediction of tachyarrhythmia episodes Proc 24th Ann Intl Conf of
35 the EMBS, Houston, TX, October 23-26, 2002: 1445-1446.
13. Thong T, Raitt MH: Ventricular tachyarrhythmia prediction. Proc 27th Ann Intl Conf of IEEE EMBS, Shanghai, China, September 1-4, 2005: 3853-3856.
14. Motulsky H: *Intuitive Biostatistics*. Oxford, UK: Oxford University Press. 1995.
15. Leenhard A, Maison-Blanche P, Denjoy I, Cauchemez B, Joubert JP, Coumel P: Mechanism
40 of spontaneous occurrence of tachycardia. *Arch Mal Coeur Vaiss* 1999; 92: 17-22.
16. Algra A, Tijssen JG, Roelandt JR, Pool J, Lubsen J: Heart rate variability from 24-hour electrocardiography and the 2-year risk for sudden death. *Circulation* 1993; 88: 180-185.
17. Task Force of the Europ Soc of Cardiol & NASPE: Heart rate variability – standards of measurement, physiological interpretation, and clinical use. *Circulation* 1996; 93: 1043-1065.

18. Schmidt G, Malik M, Barthel P, Schneider R, Ulm K, Rolnitzky L, Camm AJ, et al.: Heart rate turbulence after ventricular premature beats as a predictor of mortality after acute myocardial infarction. *Lancet* 1999; 353: 1390-1396.

Figure Legends

- Figure 1.** R-R history prior to an episode of ventricular fibrillation. This histogram is extracted from the Bio-ICD database. The patient experienced an episode of ventricular fibrillation at time 0, with detected R-R intervals under 200 ms. Shock therapy was delivered. Insert at upper left: magnified view of the tachogram from -600 to -450 s.
- Figure 2.** Cumulative distribution of the duration of the 208 records in the Bio-ICD database. The majority of the records are in the 1.5 to 2 hour range. Still 30% are less than 1.5 hour. This affects the number of predictor patterns that can be detected.
- Figure 3.** Kaplan-Meier curve for the simple acceleration pattern as a predictor of VTA. With records 0.25 hour (15 minutes) long, 44% of VTAs can be predicted. At 1.8 hours, 83% of the VTAs can be predicted. The surrogate-VA-ICD database is shown for comparison. A log rank test was performed. The relative risk was found to be 8 with a 95% confidence interval of [6.3, 10.1].
- Figure 4.** Kaplan-Meier curve for the simple acceleration pattern with the added requirement that the peak rate has to exceed 86 bpm (700 ms) as a predictor of VTA. With records 0.25 hour (15 minutes) long, 39 % of VTAs can be predicted. At 2 hours, 69% of the VTAs can be predicted. The surrogate-VA-ICD Kaplan-Meier curve is also shown. The significant reduction in the surrogate-VA-ICD curve is an indication that the peak rate requirement is a good differentiator for acceleration patterns prior to a VTA. A log rank test was performed. The relative risk was found to be 23 with a 95% confidence interval of [17.8, 30.0].
- Figure 5.** Kaplan-Meier curve for VTAPP, in the Bio-ICD database, as a function of the record length. The surrogate-VA-ICD Kaplan-Meier curve is also shown. A log rank test was performed. The relative risk was found to be 25 with a 95% confidence interval of [18.3, 33.6].
- Figure 6.** Average rate of acceleration patterns. In the calculation of the rate, each event is divided by the number of records still active at that time. Shown are the 10 minute sliding averages, along with the curve showing the number of active records. Beyond 105 minutes, the rates are not reliable due to the reduced number of records. The Bio-ICD curve, indicates a 5:1 reduction in the rate by 105 minutes. The curve for the surrogate-VA-ICD database fluctuates around the average of 0.06.
- Figure 7.** Receiver operating curve of VTAPP. The parameter being varied is the minimum R-R interval during the rhythm acceleration patterns. Sensitivity figures are derived from the Bio-ICD database. The VA-ICD database is used for the evaluation of the false positive rate. Increasing the minimum R-R beyond 700 ms yields diminishing returns.
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Table 1. Characteristics of Bio-ICD and VA-ICD database.

	Bio-ICD Database (n=90)	VA-ICD Database (n=26)
Male	89% (of 45 with data available)	100%
Age (yrs)	58.5±12.5 (in 48 with data available)	67.1±10.5
ECG length (hours)	1.56±0.77	23.5±1.3
Ejection fraction (%)	No meaningful information available	36.0±11.6
Heart disease	(of 35 with data available)	
Coronary artery disease (%)	63	85
Myocardial infarction (%)	48	77
Dilated cardiomyopathy (%)	20	19
Other (%)	17	0
Antiarrhythmic medication	No meaningful information available	
Amiodarone (%)		17
None (%)		83
ICD Indication	(of 45 with data available)	
Ventricular tachycardia (%)	63	54
Ventricular fibrillation (%)	30	31
Primary prevention (%)	2	15
Other (%)	5	0

Table 2. Ventricular tachyarrhythmia predictor performance.

Predictor	Bio-ICD database					Kaplan-Meier sensitivity (208)	Surrogate-VA-ICD database		p value: Bio-ICD vs. Surrogate – VA-ICD
	Sensitivity						False positive (Kaplan-Meier) (208)	Specificity (1-False positive)	
	Development (39 records)	Other (169)	Multiple record subjects (163)	Single record subj. (45)	All (208)				
Simple acceleration	69%	83%	76%	75%	80%	83%	43%	57%	<10 ⁻⁴
Simple acceleration with peak > 86 bpm	49%	70%	64%	59%	66%	69%	17%	83%	<10 ⁻⁴
Double acceleration	28%	57%	49%	48%	51%	57%	17%	83%	<10 ⁻⁴
Double acceleration with peak > 86 bpm	21%	53%	42%	46%	47%	53%	9%	91%	<10 ⁻⁴

Table 3. Characteristics of the false positive ventricular tachyarrhythmia prediction patterns in the control VA-ICD database.

Number of Holter records	26	
Number of episodes	20	
Average number of episodes per 24 hour	0.79	
Number of subjects with 0 episode	15	58%
Number of subjects with 1 episode	5	19%
Number of subjects with 2 episodes	3	12%
Number of subjects with 3 episodes	3	12%

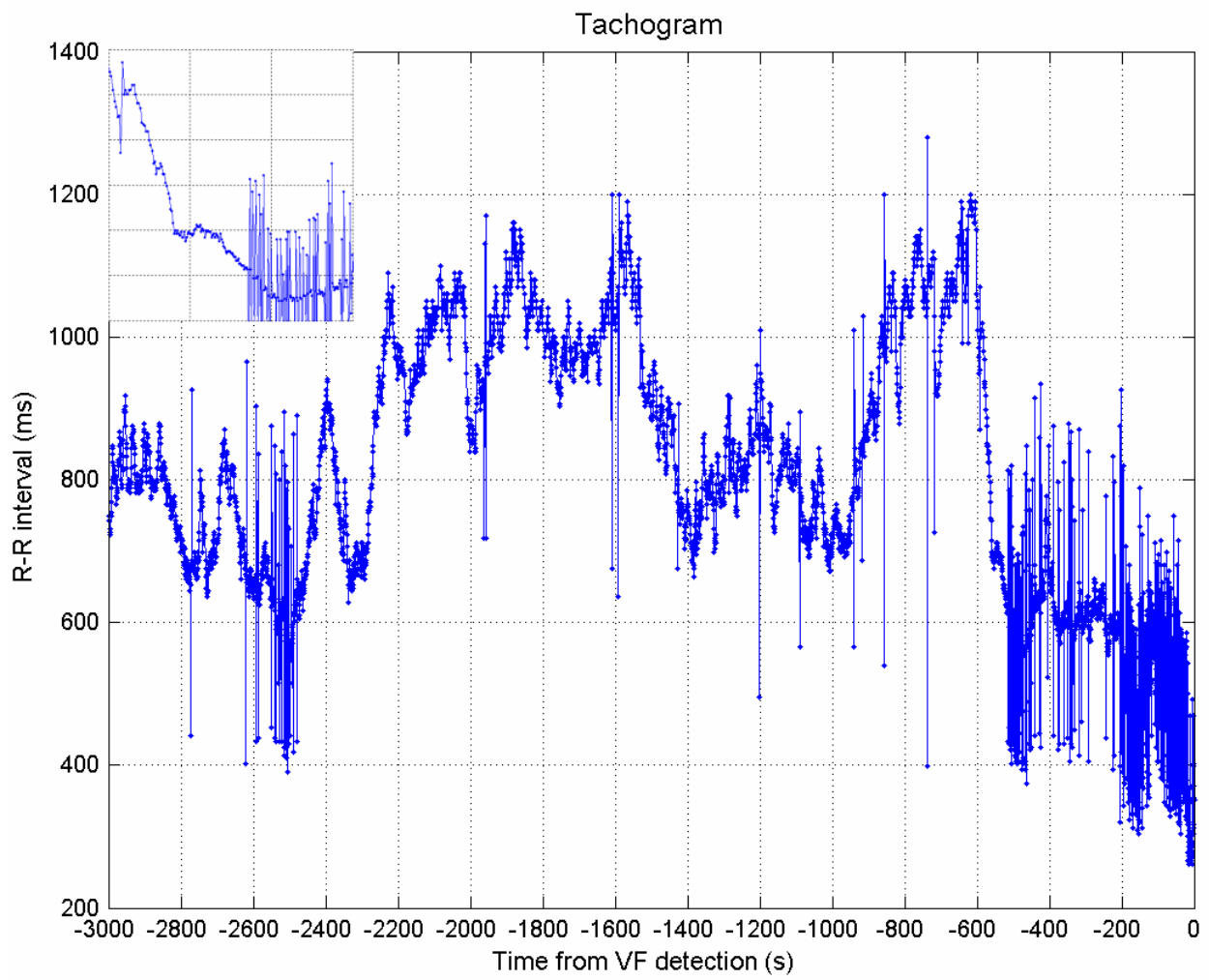


Figure 1.

Cumulative distribution of duration of 208 Bio-ICD records

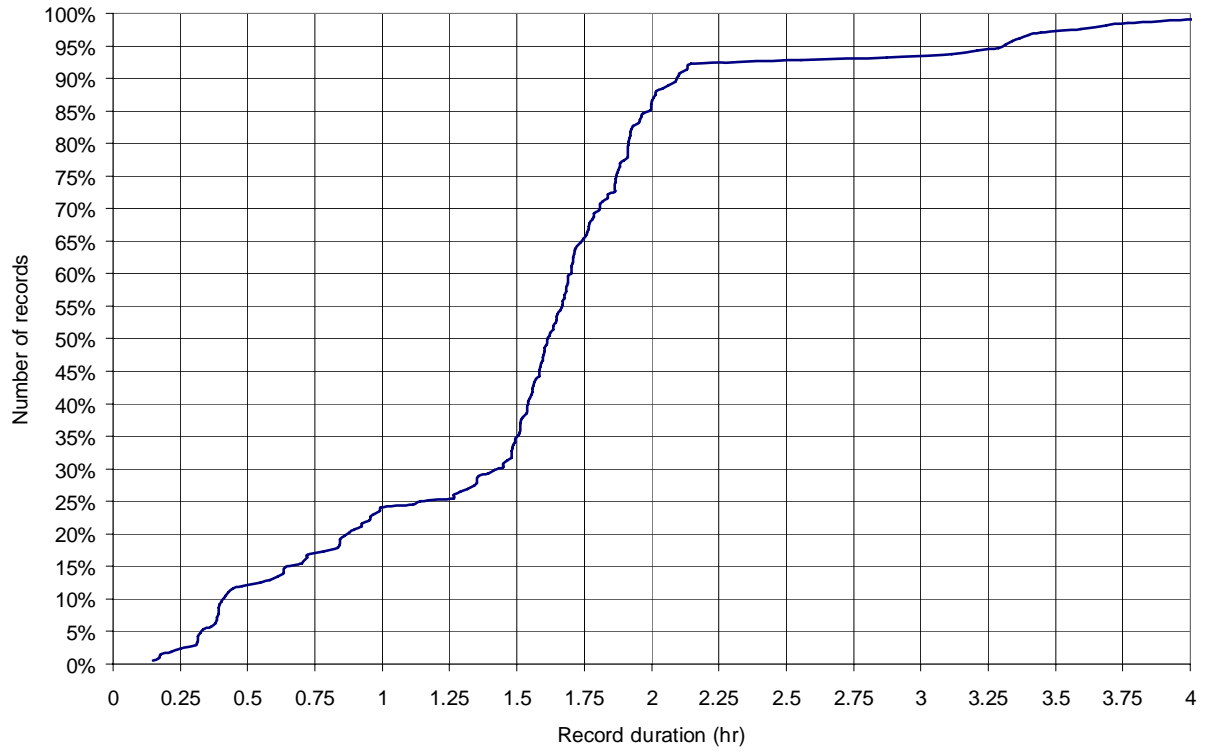


Figure 2.

Kaplan-Meier simple acceleration probability

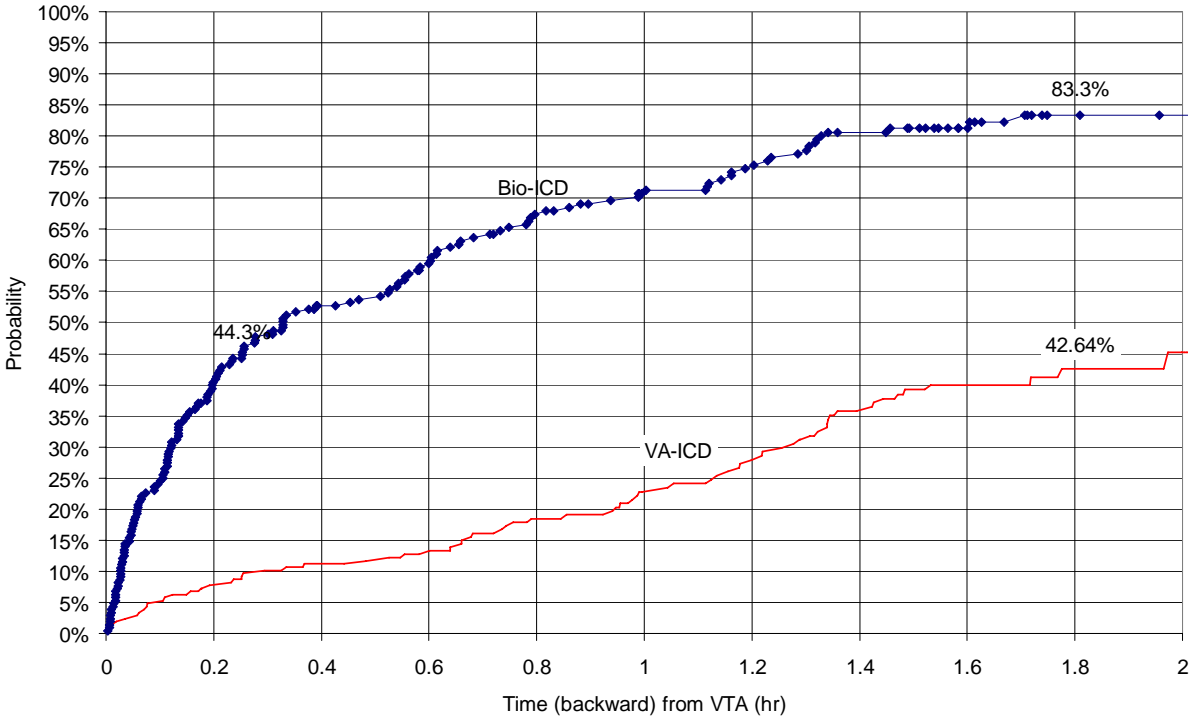


Figure 3.

Kaplan-Meier: single acceleration and peak > 86bpm

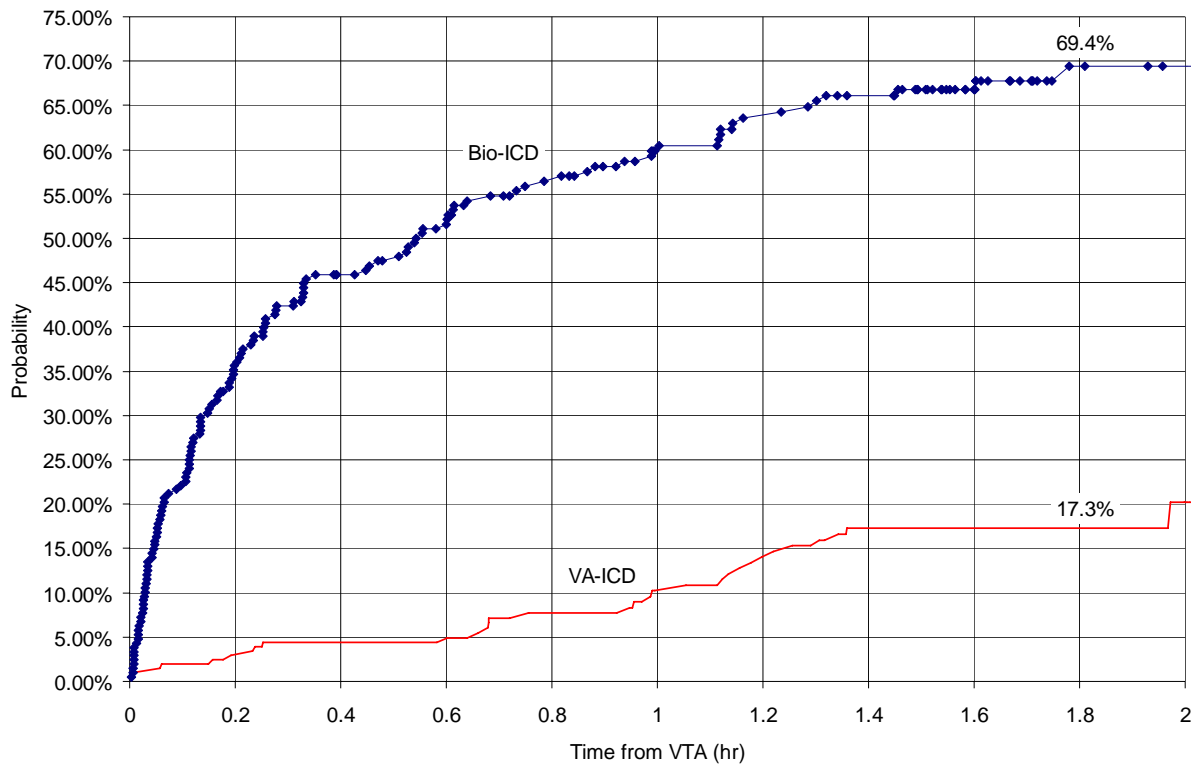


Figure 4.

Kaplan-Meier VTAPP prediction probability

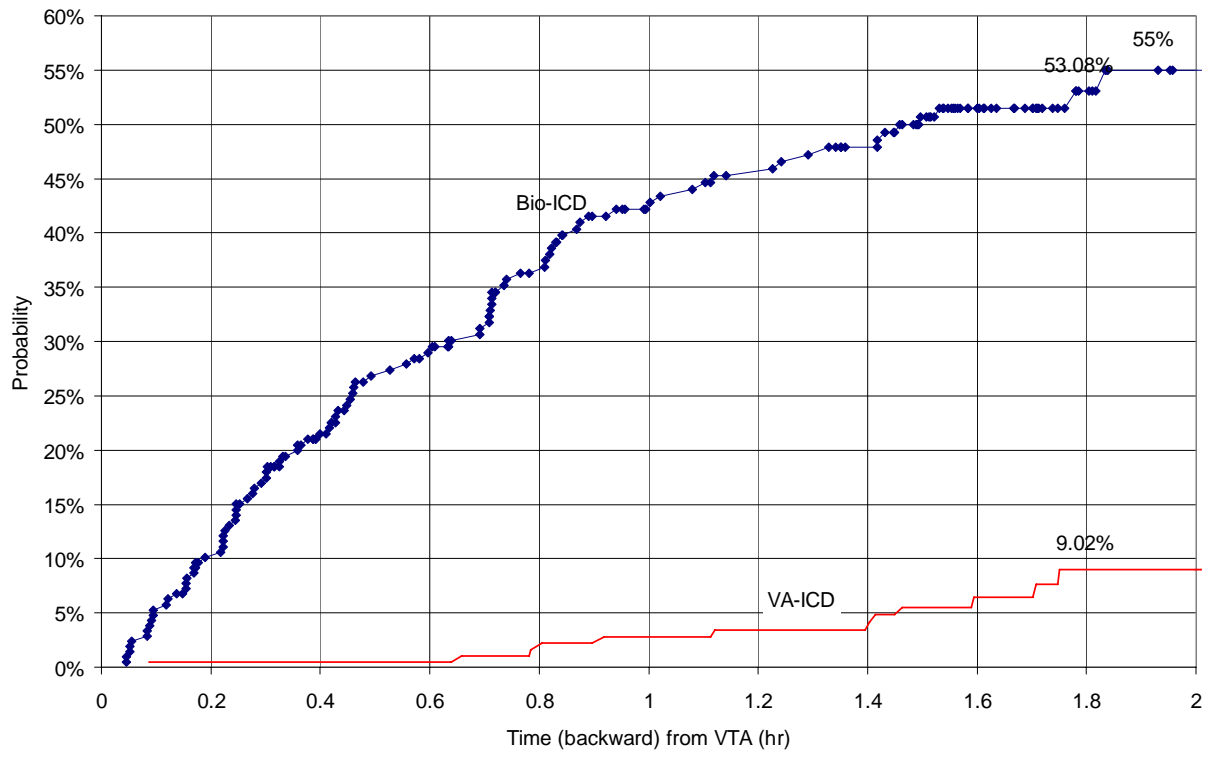


Figure 5.

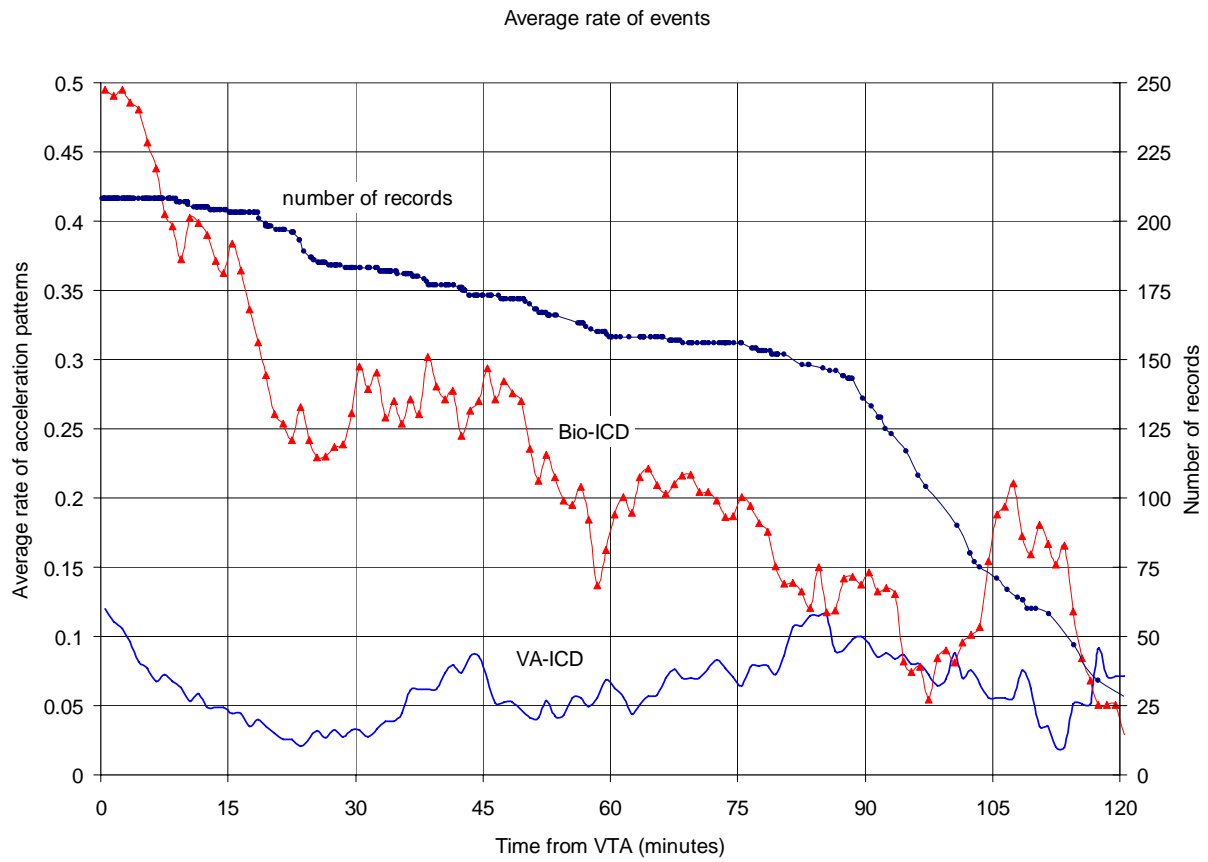


Figure 6.

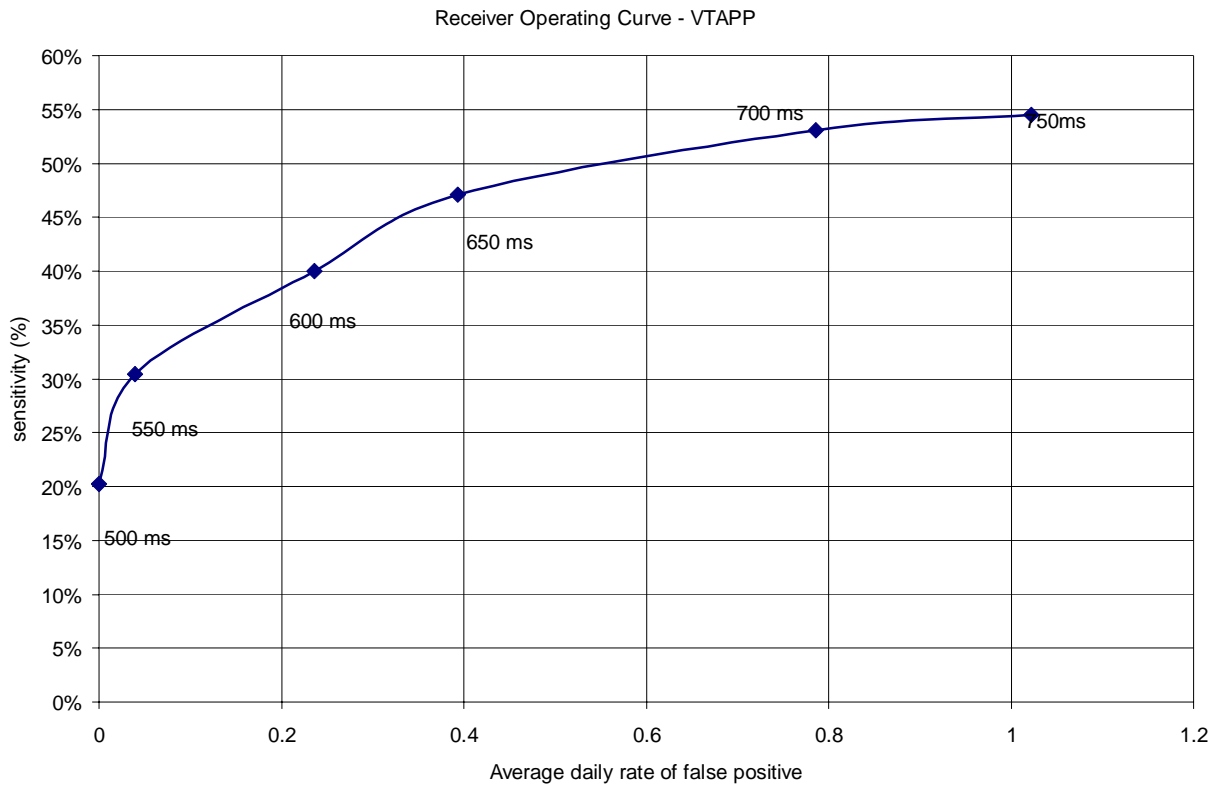


Figure 7.