MODEL-BASED ESTIMATION OF CARDIOVASCULAR REPOLARIZATION FEATURES: ISCHAEMIA DETECTION AND PTCA MONITORING

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by

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Abstract

The ST-T segment of the surface ECG reflects cardiac repolarization, and is quite sensitive to a number of pathological conditions, particularly ischaemia. ST-T changes generally affect the entire waveshape, and are inadequately characterized by single features such as depression of the ST segment at one particular point. Metrics which represent overall waveshape should provide more sensitive indicators of ST-T wave abnormalities, particularly when they are subtle, intermittent or periodic. This study discusses a Karhunen-Loeve Transform (KLT) technique for the analysis of the ST-T waveform. The KL technique was used to analyse the ST-T complexes in the ESC ST-T database. KL coefficients were plotted as a function of time, and were effective in detection of transient ischemic episodes. Twenty percent of the records showed bursts of periodic ischaemia suggesting local vascular instability. A comparison between *kl* and ST depression series has shown the KL technique as more adequate to the study of ST-T complex variations. Using the Kl series, an ischaemia detector has been developed based on a resampled, filtered, and differentiated KL series. This technique obtains a sensitivity of 65% and a specificity of 54%. These low values can be due to shifts of the electrical axis which are detected as ischaemic changes, real ischaemic episodes that were not annotated with the protocol used at the European ST-T database or erroneous detections. An increase in sensitivity can be obtained at the expense of a decrease in the positive predictive value and thus becomes a useful technique for previous scanning of the ECG record and posterior review for the expert. The technique has also been used to monitor patients during a PTCA process, demostrating that this technique allows us to monitor PTCA-induced ischaemia. A fine analysis has shown that in some cases a repetitive oscillatory behavior appears, lasting for a period of around 20 seconds, and highly related to the oscillatory behavior of the HR. In other cases, transient changes in KL series with salves behavior associated with the injection of contrast are shown on the ST-T waveform. We conclude that the KL-based analysis of the ST-T segment is a robust and sensitive technique, with considerable advantages over single feature measures in characterizing the subtle waveform changes which may be of importance in clinical risk detection.

1 Introduction

Electrocardiographic (ECG) information is derived from analysis of the information indirectly reflected on the surface ECG signal. In recent years, Considerable interest has been directed at ventricular repolarization (VR), represented at the ST-T complex, because subtle ST-T changes may be a marker of electrical instability that result in increased vulnerability to ventricular fibrillation (VF), which leads to sudden cardiac death (SCD) within minutes, without intervention. This phenomenon has a very high incidence in developed countries. Repolarization may be perturbed by multiple factors including ischaemia (which can appear as a result of Percutaneous Transluminal Coronary Angioplasty (PTCA)), structural heart disease, metabolic factors (e.g. electrolyte desarrangements, drugs) and neuroautonomic factors.

At present, there are no generally accepted non-invasive indices of risk of SCD, although such indices would have very substantial implications for both public health policy and medical practice, and many studies have sought to develop such indices as QT interval, ST level, HRV indices, etc. Most of these are derived from isolated features of the ST-T complex to describe VR, a practice that reflects the difficulty in deriving integrated measurements using visual analysis. However the ST-T waveform represents a complex spatial and temporal summation of electrical potentials from innumerable ventricular cells. Therefore, if physiologically and clinically relevant information is contained within the ST-T complex, this information may not necessarily be concentrated within any individual differential feature or sub-interval such as ST levels and QT intervals, but may be represented by the entire ST-T waveform. The proliferation

of additional "heuristic" measurements that describe the ST-T complex shape clearly demonstrates the need to consider more than the traditional measurements in order to characterize subtle changes in VR. Furthermore, noise and other sources of measurement error (such as fiducial or baseline misestimation) have far more deleterious effects on measurements of isolated features and simple differential measurements than on integrated measurements. These considerations led us to develop an analytic technique based on the entire ST-T complex using the Karhunen-Loève transform (KLT) which offers a description of the ST-T complex comprising overall information from the ST-T complex minimally affected by noise and containing maximal signal information. We propose an index (the KL coefficients) to characterize each beat[7 , 6], carrying more information than do local QT or ST indices, and thus proposing these indices as preferable to those individual measurements.

The KLT [2] is a signal-dependent linear transform that is optimal in the following sense: for any given number of parameters n, if the input is reconstructed from the first n terms of the series expansion of a linear transform, the lowest expected mean-squared error will be obtained if the transform is chosen to be the KLT. Then it concentrates the maximum signal information in the minimum number of parameters, and it defines the domain where the signal and noise are most separate. A KLT for a given type of signal must be derived from the statistics of examples of that signal. Thus, a significant limitation of the KLT is that it is necessary to collect a representative "training" set of the signals to be analysed, in order to derive the KLT basis functions (eigenfunctions). The performance of the KLT depends on how well the training set has been constructed[7 , 6].

In this study we consider two applications of the KLT technique: Detection of ischaemic episodes and monitoring processes of PTCA. Experimentally [10], one episode of ST or T variations (potentially associated with ischaemia) has been defined as implying an elevation or depression of ST level on a sequence of beats lasting more than 30 seconds. These modifications in amplitude and shape parameters have been used by Jager et al.[3] to develop an automatic detector. In that study the information was only taken from the ST level; however the repolarization alterations are reflected in the entire ST-T complex. Because of this we propose the KL analysis on the entire ST-T complex in order to evidence not only ST variations but also T wave variations. We developed a ST-T complex variations detector based on the criteria considered in [10]. On the other hand, we studied the monitoring of Percutaneous Transluminal Coronary Angioplasty (PTCA), which is used to resolve arteries affected by stenosis[11]. When the occlusion of the artery is produced by the balloon, areas of cardiac tissue are temporally deprived of irrigation and a transient induced ischaemia is then produced. Continuous monitoring of the ischaemia during the PTCA process will constitute an important aid in the follow-up of the process.

2 The Karhunen-Loève transform applied to the ST-T complex

We represent each ST-T complex first by a *pattern vector*, $\mathbf{x}$, the components of which are the time-ordered samples of the ST-T complex (after cubic spline[8] baseline correction and normalization). The KLT is a rotational transformation of a pattern vector into a *feature vector*, the components of which are the coefficients of the KLT. The first few components of the feature vector represent nearly all of the signal energy, and the remaining components need not even be computed.

The derivation of the KLT basis functions begins by estimating the covariance matrix $\mathbf{C}$ of the pattern

vectors of the training set [2],

$$\mathbf{C} = E\{(\mathbf{x} - \mathbf{m})(\mathbf{x} - \mathbf{m})^T\} \tag{1}$$

where $\mathbf{m}$ is the mean pattern vector over the entire training set. The covariance matrix reflects the distribution of the pattern vectors in the pattern space. The orthogonal eigenvectors of $\mathbf{C}$ are the basis functions of the KLT, and the eigenvalues, λ_k, represent the average dispersion of the projection of a pattern vector onto the corresponding basis function. After sorting the eigenvectors according to their respective eigenvalues, such that $\lambda_k \geq \lambda_{k+1}$, for $k = 0, 1, ..., N-1$, the corresponding basis functions are arranged in order of representational strength. The basis function corresponding to the largest eigenvalue is that function best able to represent an arbitrary pattern vector from the training set; the next function is the (orthogonal) function best able to represent the residual error obtained from fitting the first function, etc. The value of N is equal to the number of components in the pattern vector, and depends on the length of the waveform and on the sampling frequency; in this case the length is 600 ms, and the sampling frequency is 250 Hz, so that $N = 150$.

In this study, the mean pattern vector $\mathbf{m}$ can be forced to be zero, if we assume that each ST-T complex in the training set can represent both itself and its inverted counterpart. This represents the possibility that any ST-T complex may appear inverted simply as an artifact of the choice of the lead polarity when recording the ECG. Thus, the covariance matrix may be expressed simply as

$$\mathbf{C} = E\{(\mathbf{x})(\mathbf{x})^T\} \tag{2}$$

and the eigenvalues, rather than representing the average dispersion of the ST-T projection onto the associated basis function, instead represent the average energy of this projection.

2.1 Monitoring the kl series

With this methodology we have the eigenvectors and eigenvalues[7 , 6] to define the KLT representation of the ST-T complex. In clinical practice, the dynamic behavior of ST-T morphology over time is even more important than are the characteristics of an isolated complex. ST-T dynamics can be characterized by the study of KL coefficient time series (kl) using many of the techniques used in studies of HRV. We can assign to each beat mark (QRS fiducial point) the KL coefficients of its ST-T complex. In this way we will have as many (scalar) time series as there are KL coefficients needed to represent the ST-T complex. The direct way to monitor kl is to obtain it from the inner product of the KL basis with the pattern vectors of the ST-T complexes to be analysed. These pattern vectors are obtained in the same manner as those in the training set (using cubic spline baseline removal).

However, Direct estimation in this way, results in a noisy kl time series. Noise is introduced into the kl time series from a variety of sources, including noise in the ST-T complexes not removed by the KLT, misestimation of the isoelectric level (due to noise in the PR interval, or QRS fiducial misestimation), residual baseline variations, and ectopic beats not rejected. Noise in the kl time series may be reduced using an adaptive filter that removes noise uncorrelated with the ST-T complex. This technique is useful for monitoring medium- to long-term variations in the ST-T complex, such as in detecting ischaemic ST-T changes. It makes use of the recurring features of the signal and is based on the adaptive linear combiner [12].

To illustrate the interpretation of the kl coefficients in figure 1 we show a pattern of kl_0 series belonging to a ECG recording from a PTCA process. During this process the ST-T complex suffers marked variations

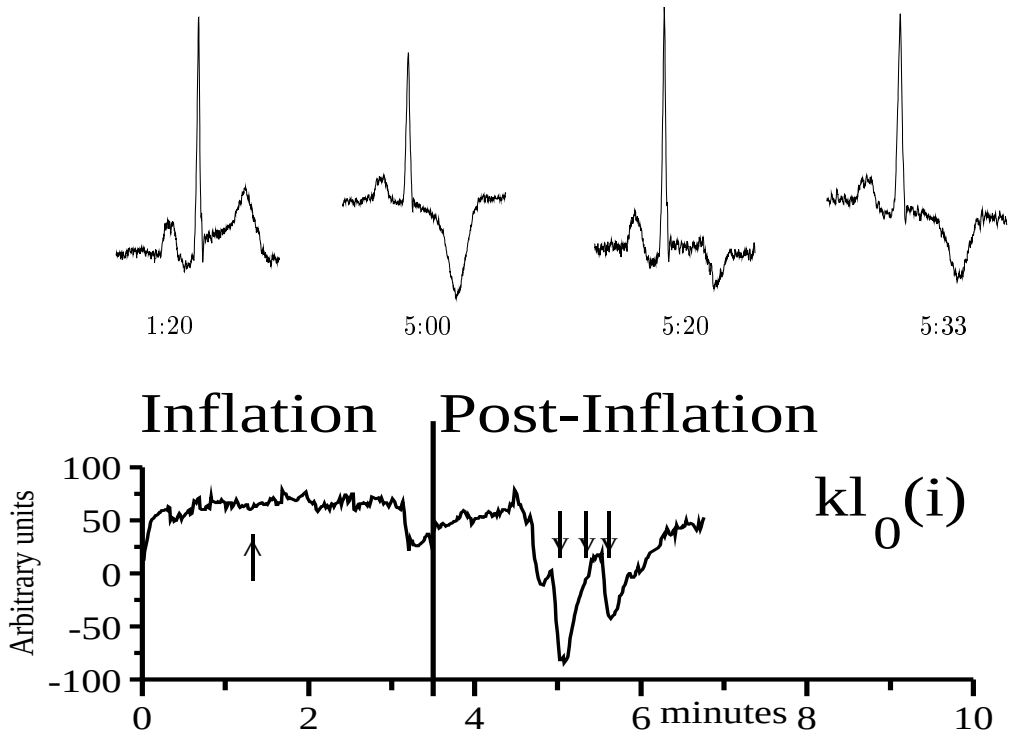


Figure 1: Example of kl series associated to large ST-T variations during a PTCA process. There are displayed 4 beats belonging to the arrowed time instants at the $kl_0(i)$ series. We can Note how at the inflation period the ST-T complex is positive corresponding to a positive kl_0 values. After inflation the ST-T complex inverts its polarity and oscillates, being this reflected at the kl_0 series as a negative oscillating value.

from inflation to Post-inflation. Superimposed on the kl_0 series are some arrows that mark the time associated to the plotted ST-T complex. We note that during the first period (inflation) the ST segment is positive and then the kl_0 is positive also. During the post-inflation period the ST-T complex inverts itself and oscillates; this is reflected at the kl_0 series as an oscillating negative value of the kl_0 coefficients.

2.2 Application to ischaemic ECG signals

In this section we present the results of estimating and monitoring the kl values on several real ECG records. Figure 2 illustrates kl time series, each 2 hours in length, for three ECG records from the European ST-T database. Figure 2a compares the kl_0 series of record e0103 for each of the two recorded ECG leads, estimated as the inner product between the ST-T complex and the KL basis function. Figure 2b shows the same series, obtained using the adaptive estimate, and showing a SNR improvement of about 10 dB compared with those of Figure 2a. Note the simultaneous appearance of ischaemic ST-T changes in both leads, but with different characteristic patterns, repeated quasi-periodically. The figure clearly shows eight ischaemic episodes, corresponding to the eight kl series peaks; only five of these are marked in the database reference annotations, since three of these episodes (1th, 2th, and 7th) are below the standard thresholds for marking ischaemic ST-T episodes. The technique we present allows these sub-threshold episodes to be clearly identified, and allows the long-term pattern of quasi-periodic ischaemic change to be observed more clearly than would be otherwise possible.

Figure 2c shows the kl_0 (left) and kl_1 (right) series of the lead MLIII (only) of record e0105, and figure 2d shows their adaptively estimated counterparts. In this case, each of the seven peaks corresponds to an ischaemic ST-T episode marked in the database reference annotations. By study of two or more KL coefficients in a single lead, we can easily monitor changes in ST-T morphology as well as changes in ST level.

Finally, figure 2e shows the uncorrected and Bazett[1] HR-corrected kl_0 time series for the first ECG signal of record e0113, and figure 2f shows their adaptively estimated counterparts[7]. As in the previous examples, the adaptive estimation of ST morphology tracks ischaemic changes noted in the reference annotation files of the database. Note the slightly higher amplitude of the peaks in the HR-corrected series, showing that the first corrected kl basis function is better able to represent the ST-T complexes in this record than is the first uncorrected kl basis function. In figure 2f, we note eight well-marked peaks that correspond to the seven marked in the database reference annotations, and one other (the second) that was not so marked, although it is quite clear from inspection of the kl series.

Analysing the entire European ST-T Database (90 records) we found that roughly 20% of the records present these quasi-periodic ischaemic ST-T changes, and that in another 20% more than one ischaemic ST-T episode exhibits a similar pattern in their associated kl time series.

2.3 $kl_n(i)$ series compared to $st(i)$ series

To show the differences between the ST level monitoring and the kl series monitoring we have estimated the ST level in several records and compared it to kl series. The weighted averaging method is used to measure the ST segment deviations. ST segments are selected from the beats aligned to the fiducial point

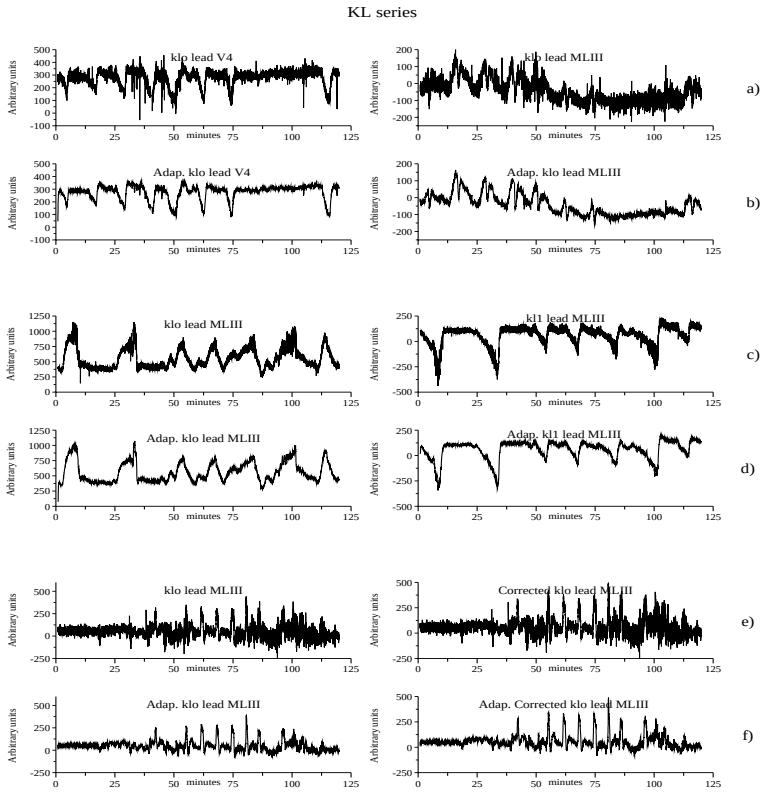


Figure 2: *kl plots for three records of the European ST-T Database. Panels (a) and (b) present* kl_0 *time series of record e0103 estimated directly from the inner product (a), and with the adaptive estimate (b); those on the left correspond to the ECG lead V4, and those on the right to the ECG lead MLIII. Panels (c) and (d) show the* kl_0 *time series for record e0105 on the left, and the* kl_1 *time series for the same record on the right. Panels (e) and (f) illustrate the uncorrected* kl_0 *time series for record e0113 on the left, and the corresponding Bazett HR-corrected* kl_0 *time series on the right.*

and are averaged each N beats. To obtain properties of convergence similar to the adaptive KL estimation method only three beats will be included in each subensemble to average. Also, only normal beats with previous and following normal beats are included in order to avoid artifacts in the estimation. The weighted averaging method is especially useful when the noise level changes from beat to beat. Each beat is added into the average with a weighting inversely proportional to its noise content[13]. Once the ST segment averaged each three beats has been constructed, the ST level is measured by taking the mean value in a 10 ms interval centered 60 ms from the QRS end.

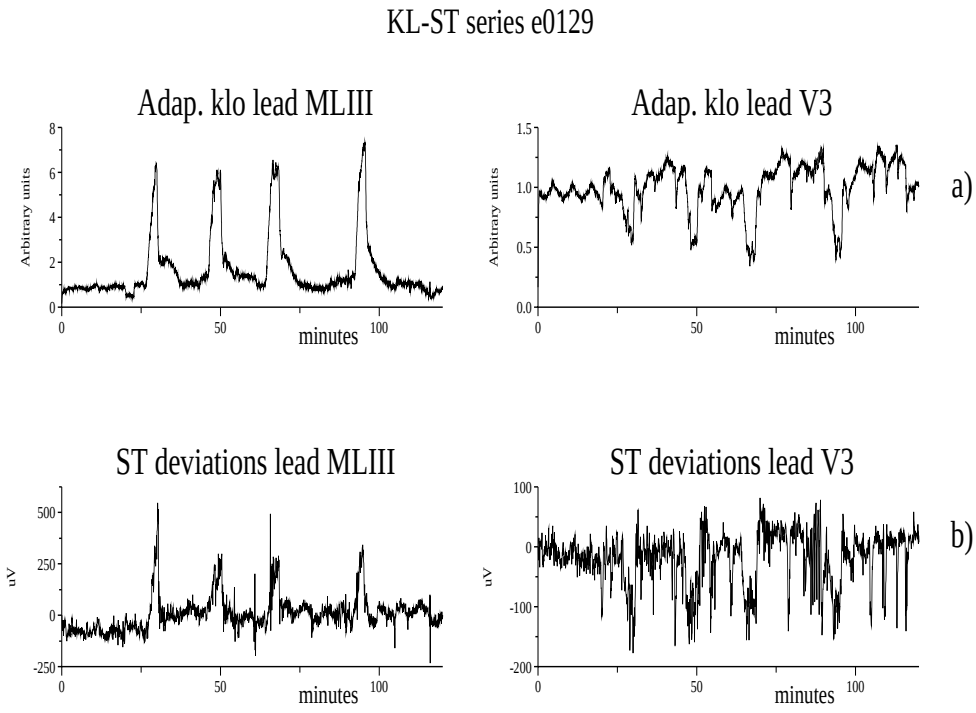


Figure 3: *$kl_n(i)$ and $st(i)$ plots for record e0129 of the European ST-T Database. Panel (a) presents $kl_0(i)$ time series estimated with the adaptive filter for lead MLIII (left) and lead V3 (right), (b) presents the $st(i)$ series for both leads estimate as described at the text.*

In figure 3a are plotted the kl_0 series of record e0129 (two leads) and in 3b the corresponding ST level series estimated as previously described. We note that in this case, where the ST episodes are clearly marked, the ST level also gives a good estimation when calculated on lead MLIII but offers much poorer results when estimated on lead V3 where kl series shows a better estimation of ST-T variations with lower noise effect.

In figure 4a we again have the kl_0 series of record e0103 (two leads) and in 4b the corresponding ST level trend. In this case, the ST level gives poor estimation of the ST-T variations but these are much more evident when using the kl_0 series. This also allows us to observe a repetitive pattern associated with the ST-T variation (potentially ischaemic episode) that cannot be clearly observed when looking at the st series. From these graphics we corroborate our expectation that the KL technique is much more robust and informative than is the single ST level measure. In addition, episodes that have not been marked by the expert annotation at the Database in one lead, but have been marked at the accompanying one, can be detected by the kl series in both leads. Record e0103 has only marked five episodes at lead MLIII and

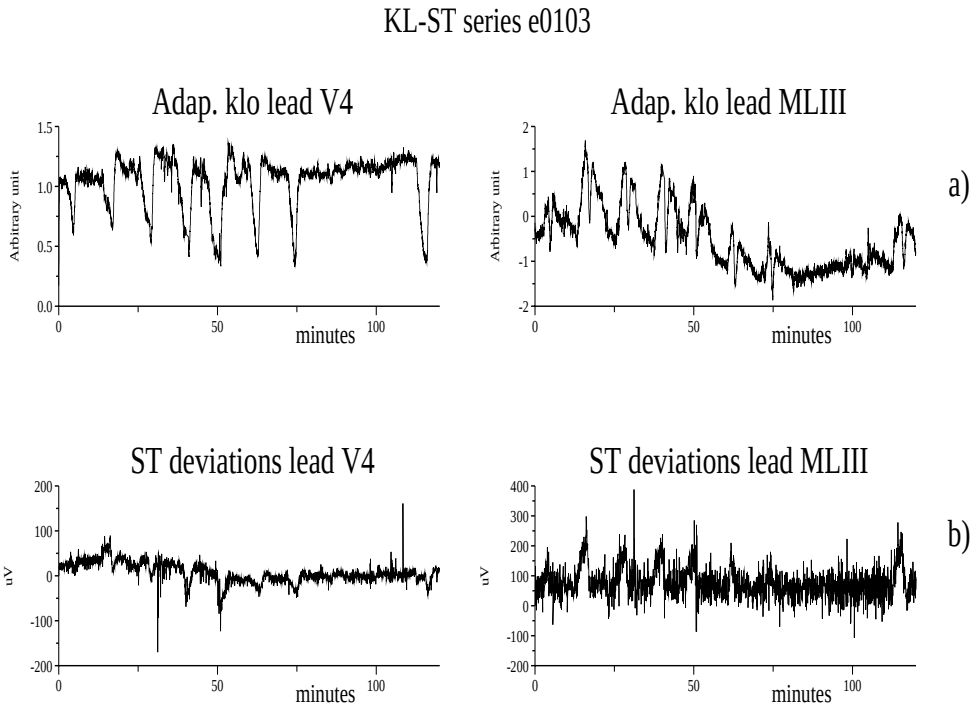


Figure 4: *$kl_n(i)$ and $st(i)$ plots for record e0103 of the European ST-T Database. Panel (a) presents $kl_0(i)$ time series estimated with the adaptive filter for lead V4 (left) and lead MLIII (right), (b) presents the $st(i)$ series for both leads estimate as described at the text.*

none at lead V4, however, at the kl series eight episodes can be observed in both leads and with repetitive pattern that make the probability of error very unlike. This observation is made recurrently observing the total records of the database, so pointing this technique as much more sensitive and information carrier than the single ST level.

3 Automatic detector of ST-T episodes

The detector that we present is based on the kl series obtained as described previously. The detector is applied over the records of the European ST-T database[9] that contain two hours of recording with two leads each one. For each lead, the two fundamental kl series (kl_0 and kl_1) have been calculated after performing the baseline correction with cubic splines. The kl coefficients have been calculated with the adaptive option to attenuate the noise effect at the ECG. In this way we have for each patient four kl series that constitute the basis of the detector.

With these four kl series, we apply a post-processing to emphasize the variations respect to a reference level. This post-processing is composed of a linear filtering stage followed by a non-linear stage and a decision criterion. The discrete kl series are resampled to a uniform sampling rate (2 Hz) since the temporal reference of $kl_n(i)$ is the one associated to the ith beat (t_i), and this is not a uniform reference as required to perform linear filtering on the kl series. We apply a low-pass differentiator to the resampled series with cut-off frequency 0.02 Hz and 60 seconds of impulse response duration. This filtering attenuates

high-frequency noise at the kl series, eliminates the DC level of the series (null gain at 0 frequency) and emphasize those episodes of fast kl variations (<50 s) that we are interested in detecting. After we apply a finite length integral (100 s) to emphasize variations up to this duration and a squaring stage to better discriminate interesting variations from noisy ones.

This process is shown in figure 5, from the kl series of record e0105 of the database. Figure 5a shows the kl_0 and kl_1 series from lead MLIII. Figure 5e shows the result of the complete processing, and the intermediate graphics show the intermediate results as described previously and marked on the graphics.

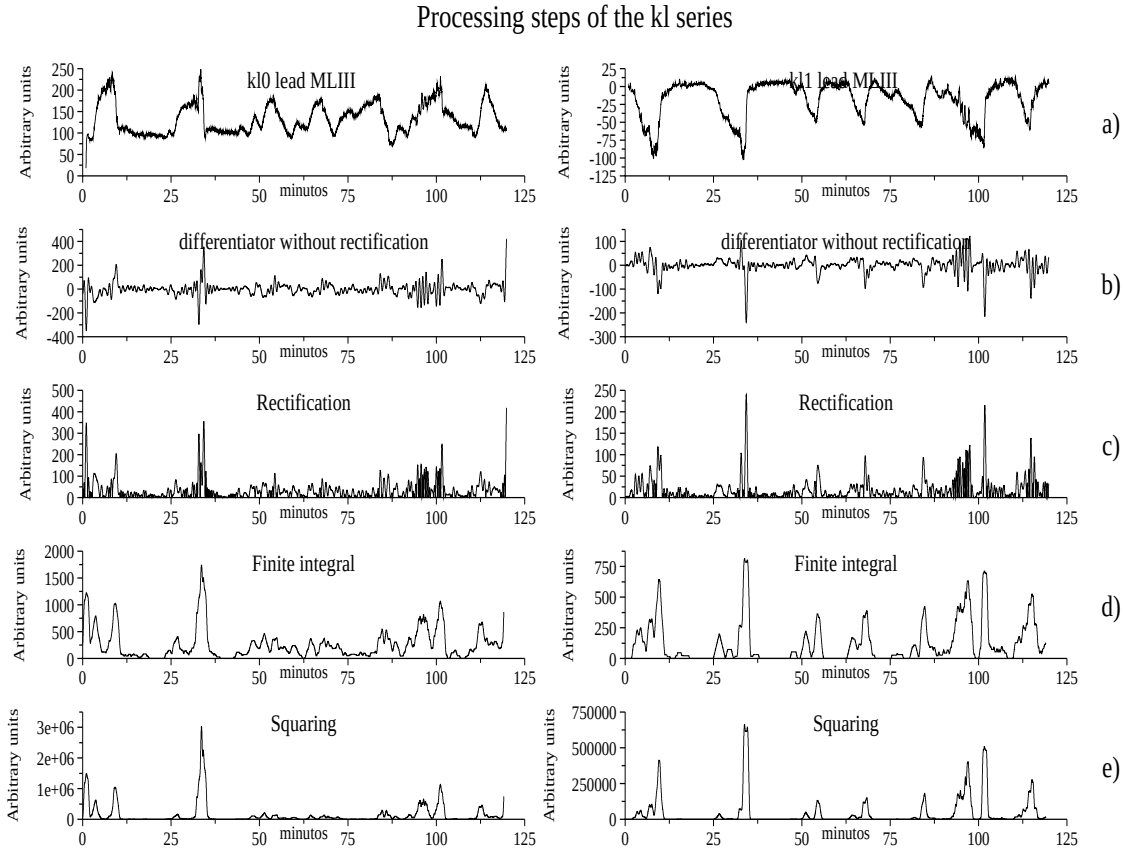


Figure 5: Processing of the kl series with intermediate results from record e0105. a) shows the kl_0 (left) and kl_1 (right) series; b) shows the differentiated of a); c) rectification of b); d) finite length integral of c); and e) squaring of d).

The process shown in figure 6, where the kl series are extracted from record e0113 of the database, shows the four processed series used for the decision criterion. Uppermost graphics (Figure 6a) are the kl_0 series from both leads and (Figure 6b) are the resulting processed series with the ST-T varying episodes remarked. Similar results are presented in figure 6c,d for the kl_1 series. In 6b (left) the threshold used to detect episodes is overprinted.

The resulting processed series are the input to the decision criterion in order to decide if there are ST-T variation episodes or not. The values of the cutoff frequency and size of the integration stage are selected in such a way that we get a better compromise between sensitivity and positive predictive values. With the four processed series we now apply a criterion to detect those episodes candidates to represent ST-T episodes variations. We interpret that one episode appears when in at least at three of the four series a threshold is crossed whose value is selected to have, again, a better compromise between sensitivity and

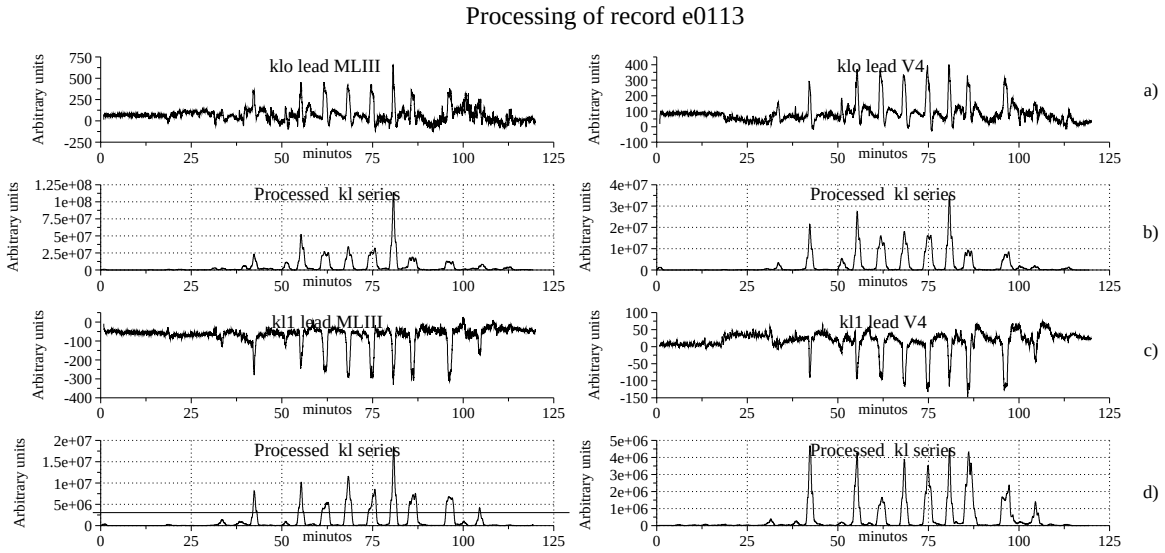


Figure 6: kl series for the record e0113. a) Shows the kl_0 for both leads; b) shows the results of processing the series to emphasize the ST-T variation episodes. c) and d) shows the same graphics for kl_1 series. At d) left is marked the threshold used to detect episodes.

positive predictive value.

3.1 Validation of the detector

The detector has been validated with the entire ST-T database. As mentioned before the records at this database were manually annotated by experts[10] and then it can be studied and compared the manual with the automatic detections. We use the sensitivity (ratio between detected true positives to total true positives) and positive predictive value (ratio between detected true positives and total detected positives) as parameters of comparison. Given same weight to the records or to the episodes we can study averaged or gross statistics, respectively[4 , 5]. Table 1 shows the resulting values when applying the detector to the entire database.

	Detected episodes	Real episodes	True detected	Sensitivity	Predictive value
Gross	322	249	164	65.8%	50.9%
Averaged	322	249	164	61.97%	54%

Table 1: Results of the ST-T variations detector applied to the entire database, see text for more details

This results, with a low predictive value, should be consider with the following restrictions:

- It has been considered the entire database, even there is a large amount of noisy records. Better quality recordings will probably increase the sensitivity and specificity.
- This detector is a tool to aid the expert not to substitute him. A posterior revision of the detected episodes will allow to classify them as noise, other misdetections or truly ST-T variation episodes.

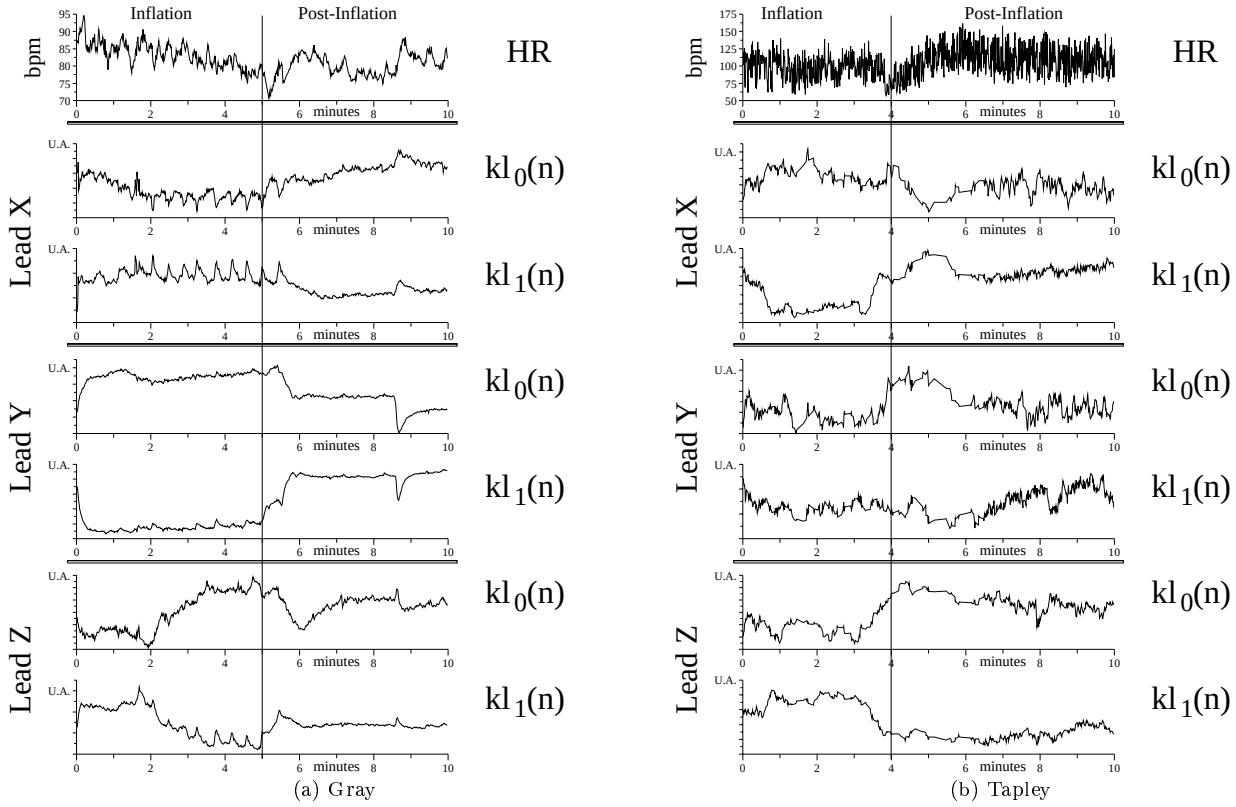


Figure 7: HR and *kl* series belonging to ECG recorded during a PTCA process. Inflation and post-inflation areas are separated by vertical line. *kl* series are expressed in arbitrary units

However this detector gives a reviewing area to the expert, that allows to reduce the work behind an exhaustive revision of the whole recordings to only review those areas indicated by the detector. Thus, is preferable to have higher sensitivity even if we reduce the predictive value of the detections.

- We can present a monitoring system of the *kl* coefficients as a supplementary diagnostic help, since we can visualize in a compact way the ST-T evolution. In this way we can contemplate episodes that by themselves could not be considered relevant but together with ST-T evolution as a whole, can be shown to correspond to phenomena with the same underlying physiological substrate. In fact we often corroborate this phenomenon of repetitive patterns where only some of them were annotated at the manual scanning reported at the database.

4 ECG analysis during PTCA

In this section we analysed the ECG recorded during PTCA. Each record is composed of the three orthogonal leads X, Y, Z, sampled at 1000 Hz with 16 bits resolution. For each patient we have several records corresponding to the inflation and post-inflation periods to analyse the ST-T variations induced by the PTCA process. The *kl* series have been represented for each lead.

In figure 7 we show the heart rate and the corresponding *kl* series corresponding to the inflation and post-inflation periods for two patients a) and b). Patient a) has suffered a PTCA on the right coronary artery;

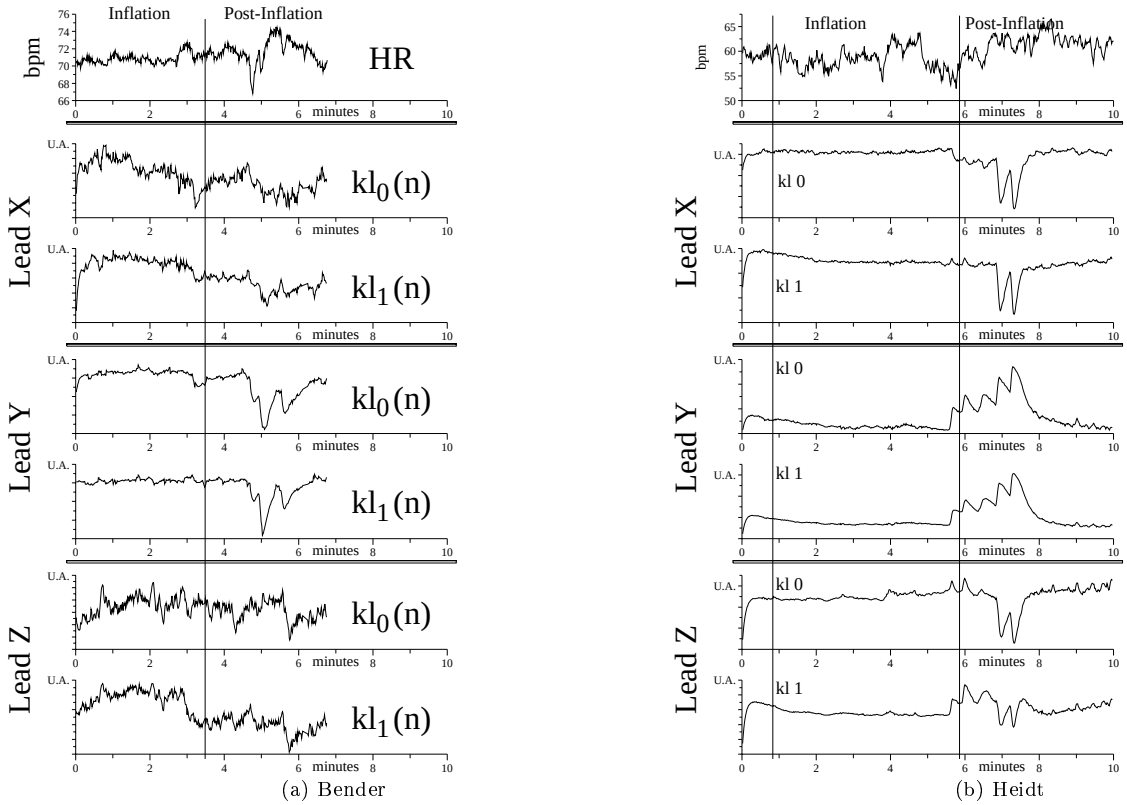


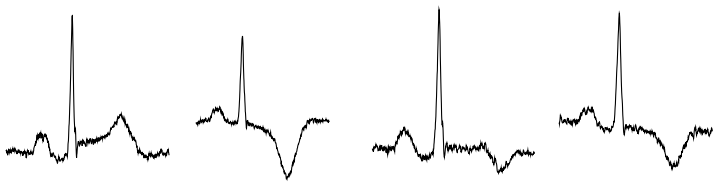
Figure 8: HR and kl series series belonging to ECG recorded during a PTCA process. Inflation and post-inflation areas are separated by vertical line. Units of KL series are arbitrary

the occlusion starts at the beginning of the record and lasts up to minute 5. During this period a depression at the $kl_0(i)$ series and elevation of the $kl_1(i)$ at lead X appears, which correspond to a depression at the ST segment. At lead Y the opposite effect is shown since there the effect is elevation of the ST segment. In both cases the variation recovers after the occlusion finishes. In this record an interesting oscillatory behavior of the kl series can also be observed during the occlusion. Every 20 seconds, periodic oscillations appear on it, and similar patterns have also been noted in the analysis of the ST-T database during some ischaemic episodes. In figure 7(b) the results for a PTCA on the Circumflex artery are shown, and similar observations can be made.

In figure 8 the results for two more PTCA recordings are shown. An interesting phenomenon appears around 1 minute after the end of occlusion. A large oscillating decay in kl_o and kl_1 appears. In figure 9 several beats are shown which correspond to the Y lead of record "Bender" (figure 8(a)) that make morphology changes clear on the ECG signal. This behavior occurs as a response to the contrast injection used to check the coronary stage after the PTCA.

5 Conclusions

In this study we applied a KLT technique for studying the repolarization period of the heart throughout the ST-T complex of the ECG signal. The KLT has been used to detect ST-T shape variations; the



(a) 1:15 (b) 5:00 (c) 5:20 (d) 5:33

Figure 9: ECG shape variation corresponding to *kl* from patient "Bender".

results demonstrate its suitability for detecting ST variations (potentially related to ischaemic events). In demonstrating the application of these techniques to analysis of the entire European ST-T Database, we have shown that about 20% of the records present a quasi-periodic pattern of ST-T varying activity, and another 20% exhibit repetitive but not clearly periodic patterns of ST-T varying changes. These numbers are obtained by analysing the graphic results (as in figure 2) for the complete set of patients at the database. These observations are drawn from information coming from the entire ST-T complex; it would be difficult if not impossible to reach similar conclusions with confidence, using classical differential measurements of ventricular repolarization such as measurements of ST level or QT interval, as was shown in section 2.3. These phenomena suggest some kind of oscillatory or periodic instability of the myocardium in those patients presenting this patterns.

A ST-T variation episode detector has been developed and its behavior has been tested at the European ST-T database. The detector shows a sensitivity of approximately 65% and positive predictive value of approximately 55%. It is far from being a robust detector but can be a great help in performing a preliminary scanning of the recordings in order to locate candidate episodes to be related with clinically significant ST-T variations or ischaemic episodes. This technique can be used for long-term monitoring of ST-T variations with posterior localized review by the clinician, or repetitive pattern identification, potentially indices for repetitive instabilities.

The application of this technique to PTCA recordings demostrates its ability to monitor the ischaemia induced by the PTCA process. It allows us to mark the evolution of the ST-T complex, either due to the ischaemia induced by PTCA or by the contrast injection. It also evidentiates any oscillatory behavior at the ST-T complex that cannot be marked with any other technique. Interpretation of this pattern from the clinical point of view is an open issue that can lead to a more profound understanding of the processes involved in ischaemia.

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