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***Abstract*—In this study, we propose a new technique which detects the anomalies in skin sympathetic nerve activity (SKNA) recorded from the chest wall by using the state-of-the-art signal processing and machine learning methods for the robust detection of myocardial ischaemia (AMI). For this purpose, a preprocessing technique that obtains SKNA from the wideband recordings on STAFF III database, which are non-invasively recorded from the skin surface of the chest wall by using an equipment that has a wide frequency bandwidth and high sampling rate, is developed. By using the data that is obtained as a result of preprocessing, a novel feature extraction technique which obtains SKNA features that are critical for the reliable detection of AMI is developed. By using the critical SKNA features, a supervised learning technique based on artificial neural networks (ANN) which performs the robust detection of AMI is developed. The performance results of the proposed technique obtained from a considerable number of patients with coronary artery disease on STAFF III database indicate that the technique provides highly reliable detection of AMI.**

***Keywords*—ECG, myocardial ischaemia, skin sympathetic nerve activity, feature extraction, classification, artificial neural networks, back-propagation algorithm, anomaly detection.**

I. Introduction

Since the invention of ECG by Einthoven, it has been an important part of clinical practice for the diagnosis of various cardiovascular diseases. A primary reason for the popularity of ECG is that it is non-invasive and can be performed in any patient by placing the electrodes to the skin to detect electrical signals from the heart. Present methods of ECG recording focus on detecting the electrical signals from the heart for the diagnosis of different cardiovascular diseases. Most of the diagnostic information in an ECG signal is contained below 150 Hz, therefore American Heart Association (AHA) recommends a bandwidth of 0.5 Hz to 150 Hz for the diagnostic monitoring of ECG signals [1]. Therefore, in conventional ECG devices, higher frequency signals that contain activities of the skeletal muscle (EMG) and nervous system are routinely eliminated by this filtering, although they are known to be clinically important [2].

Recent studies in the literature showed that it is possible to non-invasively and directly record higher frequency signals from skin surface in humans, called skin sympathetic nerve activity (SKNA), by using an equipment which has a wider frequency bandwidth and higher sampling rate [3]. The studies that investigate the relationship between SKNA and cardiovascular diseases in humans have recently started and there are a few studies that investigate the relationship between SKNA of the chest wall and cardiac arrhythmias (CA). A previous study in which simultaneous non-invasive recordings of SKNA and ECG were acquired showed that an increase in SKNA of the chest wall is associated with heart rate acceleration in ECG during CA [4]. In other words, it is demonstrated that CA is preceded by elevated SKNA, which indicates that there is a significant association between SKNA and CA. However, there are no studies which investigate the relationship between SKNA of the chest wall and AMI.

II. Methodology

In this study, we propose that application of ECG can be expanded to obtain SKNA by using the electrical signals recorded from the chest wall to perform the robust detection of AMI in patients with coronary artery disease. The proposed technique utilizes the state-of-the-art signal processing and machine learning methods to detect the anomalies in SKNA of the chest wall and provide additional diagnostic information to ECG for the reliable diagnosis of AMI.

A. Dataset Construction

The proposed technique is developed by using STAFF III database, which is a set of data acquired from patients with coronary artery disease receiving percutaneous transluminal coronary angiography (PTCA) at Charleston Area Medical Center, USA [5]. It is constructed as a result of a clinical research study performed to determine transient ECG changes during restrained coronary artery occlusion caused by PTCA, which is a minimally invasive procedure that involves insertion of a balloon that is inflated to widen blocked coronary arteries to improve blood flow to myocardium [6]. Coronary artery occlusion during PTCA induces AMI in the affected myocardial area as a result of reduced blood flow, which produces temporary chest pains together with significant changes in the ST segment and T wave of ECG [7].

The database includes high frequency ECG recordings of 108 patients acquired before and during PTCA and to date it is the largest database documenting high-frequency morphological changes in ECG during induced AMI caused by complete coronary artery occlusion. Since, the database simulates changes caused by heart attack in a clinical setting, it serves as an excellent testbed for the development of a wide range of AMI detection techniques.

Before PTCA, pre-inflation recordings were continuously acquired from all patients at rest in the catheterization laboratory, prior to catheter insertion to the coronary arteries. During PTCA, inflation recordings that started before balloon inflation and ended after balloon deflation in a major coronary artery were continuously acquired from all patients in the catheterization laboratory. Inflation recordings were annotated by medical experts to indicate the time instants for balloon inflation and deflation during PTCA, occluded coronary artery in which PTCA is performed, patient's history of previous myocardial infarction, as well as location of previous myocardial infarction.

The database was constructed by using a custom-made data acquisition equipment with an extraordinary dynamic input amplitude range. The recordings were digitized at a sampling rate of 1000 Hz and amplitude resolution of 0.6 μV, which ensured that high-resolution signals could be produced. Only patients receiving PTCA in one of the major coronary arteries were included to the database, whereas patients suffering from ventricular tachycardia or myocardial infarction during data acquisition were excluded.

B. Preprocessing Technique

In this study, a novel signal processing technique is developed to obtain SKNA by using the electrical signals that are recorded from the chest wall by means of an equipment that has a wide frequency bandwidth and high sampling rate. For this purpose, high-pass filters which have a cut-off frequency of f_c=150 Hz are designed and implemented to the wideband recordings of all patients on STAFF III database.

The performance of different high-pass filter cut-off frequency settings up to a maximum cut-off frequency of 500 Hz, which is the same as the maximum frequency component of the recordings in the database, are investigated to obtain SKNA of the chest wall. The efforts made for the optimization of the filter cut-off frequency to display sympathetic nerve activities showed that a high-pass filter setting of 150 Hz provides higher amplitude SKNA and better signal-to-interference ratio, while suppressing ECG signals. In other words, a high-pass filter with a cut-off frequency of 150 Hz has sufficient sensitivity and specificity to obtain SKNA of the chest wall. Further increases on the cut-off frequency of the filter eliminated EMG signals to a large extent, but it also resulted in lower amplitude SKNA and worse signal-to-interference ratio. Therefore, for higher cut-off frequencies of the filter, specificity of SKNA recording increased, however some part of the sympathetic nerve activities are filtered out, which reduced the sensitivity of SKNA recording.

C. Feature Extraction Technique

In this study, a novel feature extraction technique is developed for the extraction of the discriminative features from SKNA of the chest wall to perform the robust detection of AMI in patients with coronary artery disease. The critical features that are extracted from the pre-inflation and inflation SKNA are number of SKNA peaks, average SKNA, absolute SKNA and maximum SKNA.

Number of SKNA Peaks ($numSKNA$)

One of the features which is extracted from the pre-inflation and inflation SKNA is the number of SKNA peaks. In order to detect SKNA peaks, an adaptive threshold is determined for SKNA of each patient. By comparing the signal values where the amplitude of SKNA is higher than the predefined threshold, the time domain localization of SKNA peaks is performed. Fig. 1 illustrates pre-inflation and inflation SKNA peak detection of a patient in STAFF III database.

Average SKNA ($aSKNA$)

The second feature which is extracted from the pre-inflation and inflation SKNA of all patients is the average SKNA. The pre-inflation and inflation SKNA are integrated over a time window (N) and the total voltage is divided by the number of samples in the same window to obtain the average voltage of SKNA per sample, as expressed in (1).

$$aSKNA[n] = \frac{1}{N}\sum_{m=0}^{N-1} |SKNA[n+m]| \tag{1}$$

Absolute SKNA ($absSKNA$)

Another feature which is extracted from the pre-inflation and inflation SKNA of all patients is the absolute SKNA, which is obtained by calculating the summation of the absolute values of signal amplitudes for all samples of SKNA, as in (2).

$$absSKNA = \sum_{m=1}^{M} |SKNA[m]| \tag{2}$$

Maximum SKNA ($maxSKNA$)*:*

The last feature which is extracted from the pre-inflation and inflation SKNA of all patients is the maximum SKNA, which is obtained by calculating the maximum signal amplitude through all samples of SKNA, as expressed in (3).

$$maxSKNA = \max_{1\le m\le M} (SKNA[m]) \tag{3}$$

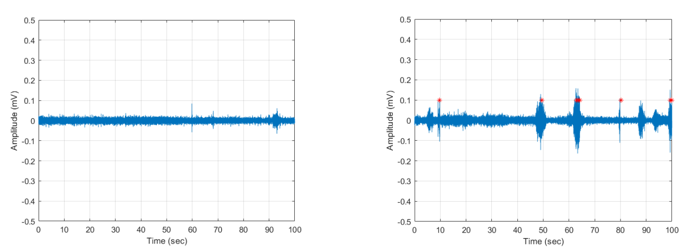

Figure 1: Pre-inflation and inflation SKNA peak detection of a patient in STAFF III database, respectively.

D. Classification Technique

In the literature, various methods have been proposed for the detection of AMI by using ECG signal. They are based on various methodological approaches which include rule-based techniques [8], artificial neural networks (ANN) [9], support vector machines (SVM) [10], fuzzy logic methods [11] and other machine learning techniques [12]. Among these methods, ANN has been successfully applied to a wide range of biomedical problems and previous studies have shown that ANN is able to accurately identify the presence of AMI by detecting the anomalies in the ST segment and T wave of ECG in patients with coronary arter disease (CAD) [13].

In this study, a novel supervised learning technique based on ANN which utilizes the critical SKNA features to perform the robust detection of AMI is developed. ANN is a nonlinear statistical algorithm which is shown to be a successful modality for the recognition of complex patterns with the ability to maintain accuracy when some data required for the network function are missing [14]. The advantage of ANN over conventional statistical learning techniques is that it can learn and model any arbitrarily complex nonlinear relationships between the independent and dependent variables [15]. If a significant amount of nonlinearity between the predictor variables and corresponding outcomes exists in the dataset, then the network automatically adjusts the connection weights in its structure to reflect these nonlinearities.

The dataset that is utilized for the development of the proposed classification technique is constructed by implementing the preprocessing technique to the wideband pre-inflation and inflation recordings of 108 patients on STAFF III database. By implementing the feature extraction technique to the pre-inflation and inflation SKNA of each patient, four SKNA features which are the most discriminative for the reliable detection of AMI are obtained. By using the min-max normalization method, the input variables are normalized to scale the features of different classes in the same range and ensure that the technique gives the same importance to data which belong to different classes.

In order to demonstrate the performance of the proposed technique on previously unseen data, the whole dataset is split into the training and test sets by using the k-fold cross-validation method. For this purpose, the whole dataset is randomly divided into k=6 equal size subsets, where one of the subsets formed the test set that is used to show the generalization capability of the technique and the remaining subsets are aggregated to form the training set that is used to train the network and optimize the parameters of the model. Additionally, the training set is further randomly divided into the training (80%) and validation (20%) subsets to prevent the technique from overfitting to the training set. As a result of repeating this process in each cross-validation fold, 6 independent training, validation and test subsets are randomly constituted.

The developed feed-forward multi-layer network consists of three layers, which are an input layer with three input units, a hidden layer and an output layer with one output unit. In order to determine the optimum number of hidden layers, multilayer perceptrons (MLP) with one and multiple number of hidden layers are developed. The experiments performed by using MLP with different number of hidden layers showed that the network with one hidden layer has shorter training time and higher generalization capability. Moreover, the optimum number of units in the hidden layer is determined by developing various networks which have different numbers of hidden units. The experiments performed with different numbers of hidden units demonstrated that the network which has 10 hidden units has the best generalization capability. On the other hand, a further increase on the number of hidden units didn't increase the generalization capability of the technique, however it increased the overall training time of the network.

The network processing is composed of the feed-forward part and the back-propagation training part, which is a supervised learning method. In the course of training, the network is constantly exposed to the training set consisting of 432 pre-inflation and inflation SKNA features for a predefined number of feed-forward and back-propagation iterations. During the feed-forward part the output of the network is calculated, while during the back-propagation training part the error in the output is used to correct the future network calculations in order to approximate the desired output. In other words, during the back-propagation training, the weights are gradually adjusted to optimize the overall computation carried out by the network in order to minimize the difference between the predicted output of the network and the known value of the outcome variable. This difference is known as the cost function of the network E, which can be expressed as in (4), where L is the number of samples in the training set, o_i is the output vector of the network and d_i is the target vector of the network for each training pair i.

$$E = \frac{1}{L} \sum_{i=1}^{L} \| d_i - o_i \|^2 \tag{4}$$

The back-propagation algorithm is a gradient-descent method to minimize the mean squared error E, where w shown in (5) is the weight vector of the weights between the layers and η is the learning rate of the network.

$$\Delta w_i = -\eta \frac{\partial E}{\partial w_i} \tag{5}$$

$$w_{(i+1)} = w_i - \eta \frac{\partial E}{\partial w_i} \tag{6}$$

Each unit of the network uses the sigmoid activation function, which is expressed in (7). The output of the network is a value in the range of zero and one, which is rounded to one if higher than a decision threshold or to zero otherwise. Thus, the resulting network output predicts diagnostic probability of the presence of AMI.

$$f(x) = \frac{1}{1 + e^{-x}} \tag{7}$$

The training length of the network is periodically tested to optimize the performance of the technique and to prevent the network from overfitting to the training data. For this purpose, after every predefined number of feed-forward and backpropagation iterations, the current weights are saved and the performance of the network is evaluated by using the validation set consisting of 108 pre-inflation and inflation SKNA features. The training of the network is terminated when the error on the validation set has reached a minimum. Therefore, the optimum network which has the highest generalization capability and the best classification performance is determined by using an independent validation set.

The performance and generalization capability of the optimum network on a previously unseen dataset is demonstrated by testing it on an independent test set consisting of 108 pre-inflation and inflation SKNA features of the representative subset of patients selected from the whole dataset. The performance of the proposed technique over the test set is evaluated by calculating the statistical performance measures, such as accuracy, detection rate, false alarm rate, positive predictive value, negative predictive value, specificity and error rate, in each cross-validation fold. The performance results calculated for each performance measure at different cross-validation folds are then averaged to produce a single estimation that represents the classification performance of the optimum network. Table I demonstrates the performance results of the proposed technique for the optimum network and critical joint SKNA features, which are $numSKNA$, $absSKNA$ and $maxSKNA$.

III. Results and Conclusions

In patients with AMI, temporary chest pains together with changes in the ST segment and T wave of ECG may occur before the onset of myocardial infarction. However, quite large number of patients in the world suffer from silent myocardial ischaemia, which means that they don't demonstrate the common symptoms of AMI and there are no explicit changes in the ST segment or T wave of their ECG signal. Therefore, it is not possible to perform the reliable diagnosis of AMI by utilizing the diagnostic information of ECG in these patients.

In this study, a new technique which uses the state-of-the-art signal processing and machine learning methods to detect the anomalies in SKNA is developed to perform the robust detection of AMI in patients with coronary artery disease. The proposed technique demonstrates the first findings related to the changes in SKNA of the chest wall over the course of induced AMI caused by complete coronary artery occlusion. The performance results of the proposed technique which employs the optimum network and critical joint SKNA features obtained from a considerable number of patients on STAFF III database indicate that the technique provides highly reliable detection of AMI. Therefore, in cases where the diagnostic information of ECG is not sufficient for the reliable diagnosis of AMI, the proposed technique can be used to expand the application of ECG to detect the anomalies in SKNA of the chest wall. The utilization of the anomalies in SKNA as an additional diagnostic feature to the anomalies in the ST segment and T wave of ECG can significantly increase the detection performance of AMI, as well as various other ischaemic heart diseases. Thus, the contribution of the proposed technique to the reliable diagnosis of AMI can be much higher than conventional ECG devices and the utilization of SKNA for the diagnosis of ischaemic heart diseases can gain a new perspective.

TABLE I: The Performance Results of the Proposed Technique for the Optimum Network and Critical Joint SKNA Features (%)

Performance Measures	***Performance Results (%)***
Accuracy	80.56
Detection Rate	77.78
False Alarm Rate	16.67
Positive Predictive Value	82.35
Negative Predictive Value	78.95
Specificity	83.33
Error Rate	19.44

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