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Development and performance evaluation of a coronary artery disease prediction system with transfer learned model based on single lead and multi-lead ECG & TMT-ECG signals

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***Abstract*---**Coronary artery disease is one of the major cardiovascular diseases and is a cardiac condition where plaque formed in arteries leads to death worldwide. The identification of CAD in the traditional

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approach needs a report of ECG, TMT ECG, Pharmacological test, and echocardiogram. The confirmation of CAD leads to undergoing cardiac catheterization. An effective prediction system that can detect the existence of CAD with an initial test like ECG or TMT ECG report image will act as a good assistance to doctors and patients undergoing periodic health monitoring. The present study is focused on developing a prediction system for CAD disease based on raw and filtered, single lead and twelve lead ECG signal images. The algorithm results are compared with transfer learning algorithms. The novelty of the work is highlighted by the fact that the prediction accuracy of the developed algorithm, with single lead and twelve lead ECG or TMT ECG signals (accuracy of approximately 93.5% for single lead and 94.5% for twelve lead) is much higher compared to transfer learned algorithms. The developed model exhibited better accuracy with lesser number of layers compared to deeper pre-trained algorithms. Further, an user-friendly GUI (Graphical User Interface) is developed based on proposed algorithm to support healthcare experts in classifying CAD ECG signals without much effort.

***Keywords*---**ECG, TMT-ECG, prediction algorithm transfer learning, pre-processing, GUI.

Introduction

Coronary Artery Disease (CAD) is a cardiac condition in which fatty compounds called plaque buildup within the artery walls and block blood flow to the heart muscles. A plaque is the buildup of calcium phosphate ($Ca3(PO4)2$) and fat in the arteries, which leads to atherosclerosis [1]. This will cause a restriction on blood flow and affect the performance of the heart. In the United States, coronary artery disease (CAD) is responsible for around 610,000 deaths each year (nearly 1 in every 4 CAD patients). It is also stated that this heart ailment is the third leading cause of death across worldwide (17.8 million deaths per year) [2].

There are a variety of diagnostic tools that can be used to detect CAD, such as electrocardiogram (ECG), exercise stress test (Treadmill test (TMT)), echocardiogram, pharmacological test, and Cardiac catheterization (angiogram). Cardiac catheterization is a time-consuming and invasive procedure requiring experts for inserting a catheter into the arteries to remove plaque formation[3]. Electrocardiogram and Tread Mill Test (TMT-ECG) are the usual techniques for the initial examination of the heart. These will help doctors to assess the cardiovascular problems, abnormal heartbeat and identify the requirement for cardiac catheterization.

A 12-lead ECG test involves gathering information about the heart with 10 electrodes placed around the heart during the resting condition. The electrical activity of the heart is monitored during walking on a treadmill test (TMT-ECG). The treadmill speed is increased throughout the test in accordance with the Bruce protocol. The results demonstrate how well the heart responds to different levels of exercise-induced stress [4]. Specific heart disease is diagnosed based on the variations detected in the ECG signals. Identification of minute changes in ECG and TMT ECG signals and interpolation needs the knowledge of experts. This will be a major challenge during periodic health checks of people in remote areas. As a result, TMT ECG (stressed ECG) [5] aids in overcoming these issues, and computer-aided diagnostic methods are used to boost the accuracy of cardiac health diagnosis by detecting minute fluctuations in ECG signals.

Several researchers have focused on CAD to improve diagnostic tool efficiency by using either normal ECG or exercised ECG recordings. During ECG signal analysis in normal and CAD people with Aartificial Intelligence, the linear and non-linear approaches are developed[6,7]. But, Cardiologists examine time-domain elements (ECG features) such as T and Q wave amplitudes, and ST level segment fluctuations as indicators of heart illness during traditional medical conditions[8]. ECG analysis utilizing time-domain characteristics is challenging due to noise and the lack of knowledge of healthcare professionals. An intelligent system with effective signal pre-processing techniques before feature extraction is necessary to successfully extract time-domain properties from ECG [9]. The time-domain properties of ECG signals do not provide crucial information on non-linear interrelationships. As a result, non-linear features are recovered, which handle the inherent complexity of the time series and reveal the non-linear behavior of ECG signals[10,11], which may be efficiently dealt with a computer-aided prediction system.

There are large repository datasets available related to heart diseases such as arrhythmia (MIT-BIH [12], Physio-bank competition 2017[13]), Arterial fibrillation [14], and cardiovascular diseases such as CAD [15], but compared to the first two, coronary artery disease-related datasets are scarcely found. The available repository dataset are 8 CAD patients and 11 normal patients dataset[16]. Based on this, the construction of a generalized prediction system will be a difficult task that can be sorted out with a vast amount of data collection. This extends the present work to gather the dataset (in an ethical way) for the analysis and development of a generalized prediction model.

A simple neural network (NN) [17] consists of an input layer, a single hidden layer, and an output layer. Deep learning [18] is the application of more than one hidden layer in a simple neural network, which has the advantage of being able to recognize more complex information because of its numerous hidden layers. Additionally, DNN can manage big data and large dimensional data which include several features.

CNN (Convolutional Neural network) is a popular form of DNN that is commonly used in nonlinear problems. The CNN model effectively deals with the sound recordings of normal and abnormal heartbeats (82% accuracy). The use of CNN has been extended in the field of detection of arrhythmia (79% accuracy) [19] and atrial fibrillation (80% accuracy) [20]. Even CNNs are effectively applied for automatic CAD recognition, and it has been discovered that CNNs remain powerful despite moving and scaling invariance, making them advantageous [18].
There are well known pre-trained models such as VGG16, Inception, MobileNet, ResNet, and EfficientNet based on the transferred learning approach. The

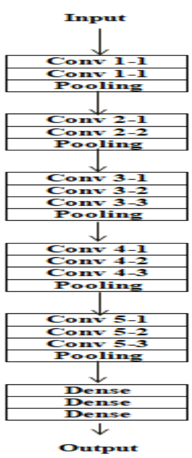
application of the pre-trained models is also well established in the field of medication, to identify and classify the disease effectively, are discussed further.

VGG16

The model is based on a convolutional neural network derived in 2014. It is one of the best vision model architectures. Instead of dealing with large data and the huge number of hyper-parameters, VGG16 appears to focus on a tiny convolution layer with filter size (3x3) and stride one. Even, the padding and max-pool layers have filters(2x2) and stride two. A similar arrangement is repeated throughout the complete architecture, at the end of the architecture it is connected to the output followed by fully connected layers. For the classification, the output layer is coupled to a sigmoid activation function. The number 16 in VGG16 refers to the number of weighted layers contained in the network, which has around 138 million parameters. [21,22]. Transfer learning method is used to get a pre-trained configuration of VGG16 architecture (figure 1) with the ImageNet dataset to predict the present ECG signal image dataset. Initially, the architecture model is trained with a large labeled image dataset (1.4 million) with thousand different classes. This helps to get a good pre-trained model and feature learned model to classify ECG signal images.

MobileNet

Is a Google-built model architecture to give real-time categorization capabilities in devices such as smartphones with limited computational capabilities. The network architecture uses an inverted residual structure as the input and output of the residual block are like thin bottleneck layers. It also employs lightweight convolution filters to improve the features in the expansion layer and reduce non-linearities in the narrow layer. This leverage implementation was carried out using a transfer learning approach from ImageNet data to a present dataset. [23]. This MobileNet improves the efficiency based on the state-of-the-art performance of mobile models across the spectrum of different model sizes. The overall architecture of MobileNet is represented as shown in figure 2.



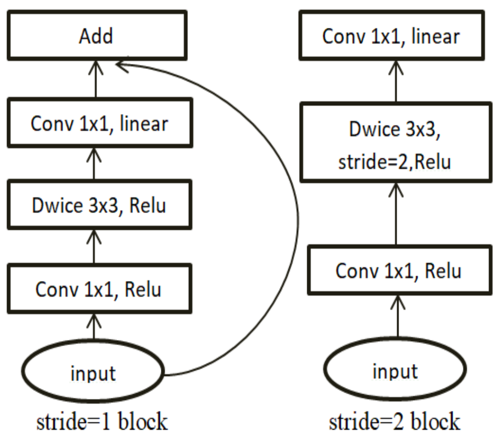


Figure 1: Architecture of VGG16 Figure 2: MobileNet Architectur

Inception

Inception is a more advanced version of GoogleNet [24], which was first demonstrated in the ImageNet recognition competition. Using the transfer learning [25] approach, the network also obtained good classification performance in numerous biomedical applications. The inception model is used to integrate many convolutional filters of varying sizes into a single filter, minimizing the amount of parameters that must be learnt. (i.e. during a deeper network with controlling parameter under 25 million (inception) better compared against 60 million for AlexNet[26]). This results in a reduction of computational complexity throughout the network. Figure 3 depicts the overall architecture of inception.

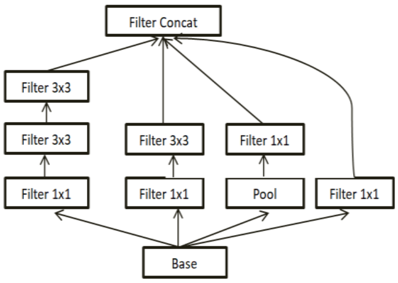


Figure 3: Architecture of Inception

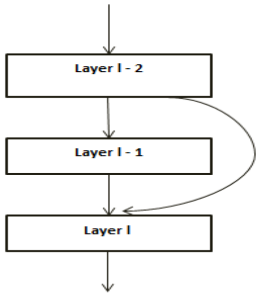


Figure 4: Canonical form of a residual neural network.

ResNet

Residual neural networks are another well-known network for transfer learning (ResNet). This network utilizes skip connections, shortcuts, and bypass links to optimize layer weights. The non-linearity activation function (ReLu) and batch normalization are incorporated in the middle layers of the architecture in general ResNet models [27]. The extra weight matrix may use to train or learn skip weight method adaptation, hence this model is also called as Highway Nets[28]. Figure 4 illustrates the Architecture of ResNet.

EfficientNet

The EfficientNet is a family of CNN-based architectures developed by the google team. The EfficientNet is a part of the baseline model neural network developed based on the ImageNet dataset. This architecture not only improves the accuracy but also provides better efficiency by reducing the number of parameters as compared to the state-of-the-art methods. There are several models developed deriving from baseline models by performing compound scaling methods(EfficientNet B1 to B7) [29]. Figure 5 depicts the baseline efficient model.

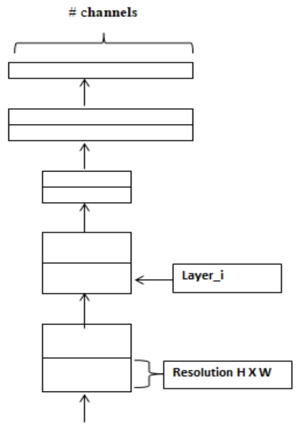


Figure 5: EfficientNet baseline architecture.

The proposed work focuses on the development of a predictive system for neighborhood hospital (KMC-Mangalore, India). The data from the hospital is in the scanned ECG signal images that include single lead and twelve lead. The signal images are pre-processed by removing noise and string values printed in the image. The images are corrected for classification with Skew-detection based on Hough transform, color-based image segmentation using OpenCV, and multi-crop. A CNN model is developed for image classification to diagnose CAD and build an intelligent predictive system. The work focusses on firstly to evaluate the developed algorithm behavior in noisy (raw) signal conditions and pre-processed (filtered) signal conditions. Secondly, to compare the accuracy of the developed algorithm with pre-trained algorithm (VGG16, Inception, MobileNet, ResNet, EfficientNet) generated by transfer learning methods. The results of the pre-trained algorithm and the developed algorithm are compared in terms of training loss and accuracy. These outcomes are derived from raw(noisy) signal images and filtered images under consideration of both single and multi-lead(12 lead) signal images. The structure of the paper is as follows, Section-I. Introduction, Section-II. Materials & Methodology, Section-III proposed CNN model, Section–IV pre-trained model, Section-V Results & discussions, and Section-VI conclusions.

Materials and Methodology

Dataset

The research focused on the development of a prediction system for twelve lead ECG and TMT ECG signal images and single-lead ECG and TMT ECG signal images. In this study data is fouced on patients who are residing in remote areas (rural area), were ECG and TMT ECG report images are dispensed. The ECG information is gathered from a well-known nearby hospital that specializes in cardiac problems (KMC Mangalore, Karnataka, India). The data set includes horizontally scanned signal images of 236 healthy volunteers and 316 CAD patients (considering male and female patients) with angiography confirmation. A 12-lead ECG in resting state and a TMT ECG image for normal and CAD participants are shown in figure 6. The collected datasets are 1sec duration signal of each lead. This will help to identify the disease in a short time. The analysis is carried out with consideration of raw signal images and filtered signal images. The raw signal images are the images which are directly obtained from scanned images without undergoing any pre-processing methods. The pre-processed (filtered) image signals are derived from raw signal images, through a sequence of steps, described in the section below.

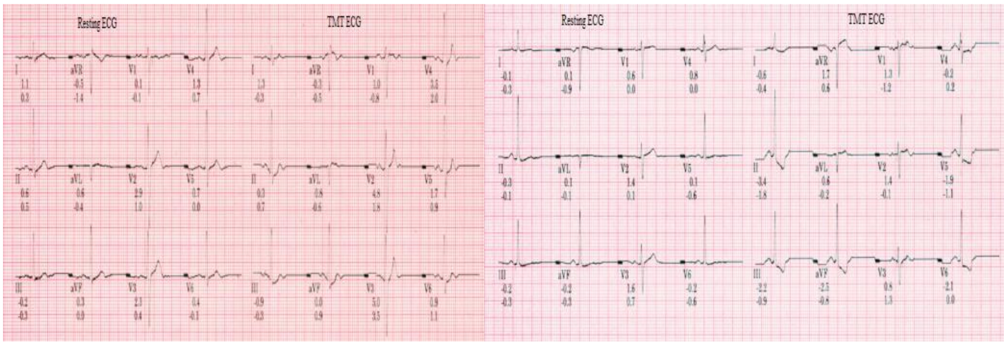


Figure 6: The scanned paper ECG of 12 lead signals for normal (Left) and confirmed CAD (Right) which has resting and treadmill test ECG signal images.

Pre-processing

The raw image was filtered out during the pre-processing stage in order to obtain a clear signal image. This pre-process includes skew detection and correction (scanned image orientation correction), color-based image segmentation for background removal (grid removal), application of a median filter to remove salt and pepper noise, printed text detection using easy OCR, and application of OpenCV to erase the text, image dilation to improve pixel quality, and multi-cropping based on single lead image position by giving height and width. The pre-processing step assists in obtaining the whole dataset (i.e., single lead raw and pre-processed (filtered) image and 12 lead filtered images) that is needed to develop the prediction algorithm. The detailed procedure of pre-processing methods is depicted in figure 7.

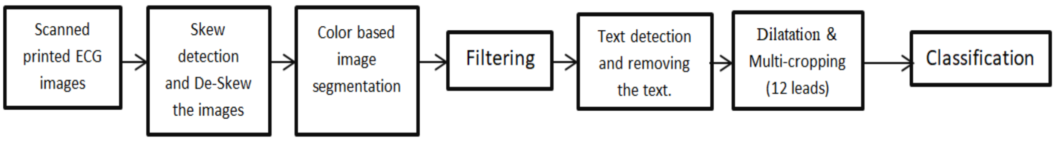


Figure 7: Overview of the block diagram related to pre-processing.

Initially, Skewed images are slanted images that are typically found in scanned/captured photos. which negatively impact on accuracy. One of the finest methods for de-skewing an image is to use the Hough transformation(which is a basic linear transformation function.) [30]. The background grid lines of the scanned ECG image are used to compute the skew rotation angle of the image. A straight line can be detected using the Hough transform. As a result, the straight-line Z = bx + c (where b is slope and c is intercept point) can be represented in the Hough space as a point (c, b). Using the transform function as in equation 1[31], every point (x, y) in cartesian space is mapped into a sine curve in $\rho - \theta$ Hough space.

$$\rho = x \cos\theta + y \sin\theta \text{-------------} \quad (1)$$

After deskewing, color based image segmentation is used to eliminate the background of an ECG signal image (figure 8a) . Background grids are often lighter in shade compared to ECG signal images. The image is processed column by column, and each column's darkest pixels are replaced with black pixels, while the remaining pixels are kept as white pixels. This results in binary image formation (figure 8b) [32].

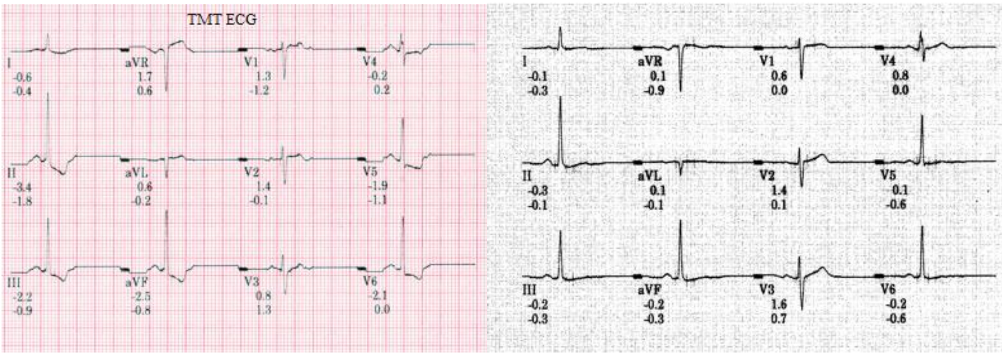


Figure 8. (a) Original Image and (b) Binary ECG image with noise

The removal of background degrades the actual ECG signals due to the presence of noise called salt and pepper noise. To avoid fault diagnosis, it's important to minimize the noise effectively using filters. Visual inspection [33] yields the best results when a median filter is used to remove the majority of the noise. This image filtering technique scans the image with a tiny matrix and recalculates the center pixel value by taking the median of all pixel values within the matrix. The resultant image is shown in figure 9.

Text Detection and removal helps to remove the undesired string element pixels that do not correspond to the signal image (Printed characteristics not considered for analysis). Optical Character Recognition (OCR) is a useful technique for converting text in photographs into computer-readable text (figure 9). In addition to this, CRAFT [34] algorithm is used for detecting phase with the help of CRNN Recognizing model. It consists of three main phases which are considered feature extraction, sequence labeling, and decoding. Based on the character location score and character affinity score which are generated by the easy OCR method will help to fully cover various text shapes over the image in a bottom-up approach. Inpainting operation (using Navier-Strokes algorithm) developed using OpenCV helps to remove the recognized text. Deletion of text requires masking the original image where the text has to be erased. To achieve this, the dimensions of the mask image and the input image must be the same. The mask will show non-zero pixels(detected text) indicates text and would be in-painted[35], while zero pixels(signal image) will remain unchanged(figure 10).

Once printed text is removed, application of morphological operation (dilation) that helps to improve the image features with consideration of 2 inputs. One of the inputs is related to dilated image and the other one corresponds to a two-dimensional image. The dilation also helps to amplify features in the signal image[36]. And the multi-cropping method makes it possible to extract single-lead ECG and TMT ECG signal images from 12-lead ECG and TMT ECG signal images. The OpenCV is used to crop each individual lead by determining the lead image's dimensions.

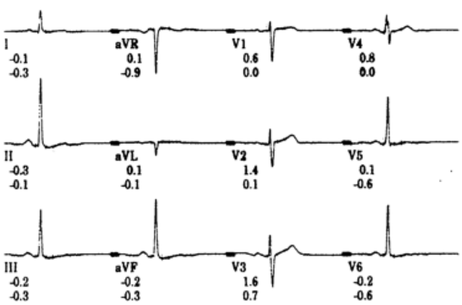


Figure 9. Filtered ECG image

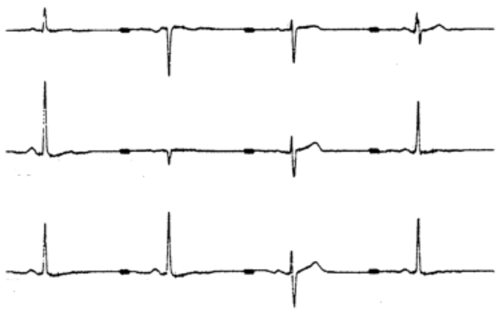
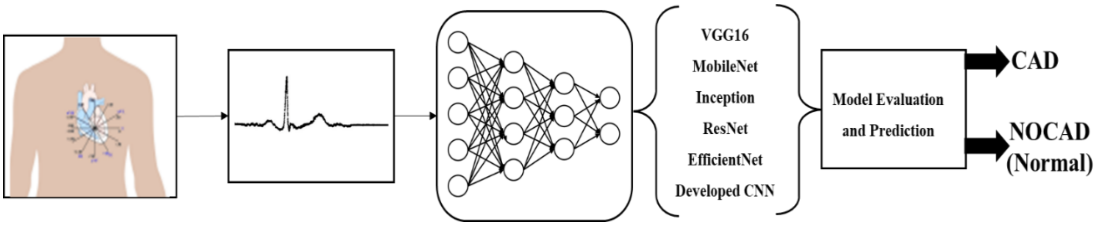


Figure 10: Text erased ECG image

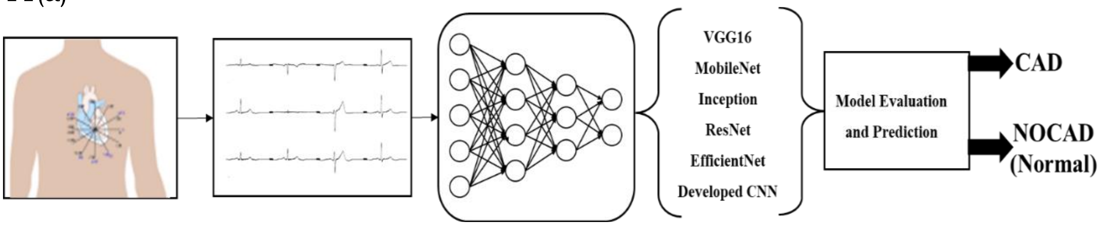
Prediction System

The prediction system is developed with the help of a deep learning algorithm, to predict CAD disease. Since Convolutional neural networks are more suitable to deal with image based datasets, a deep learning model is used to develop a prediction system for ECG and TMT ECG signal images. This prediction system is primarily developed in Python utilizing Keras with TensorFlow backend and Sci-Kit learn modules. The power of the Graphical Processing Unit (GPU) is exploited in the developed algorithm for image processing, thus saving computation time. The proposed network model is developed, accounting for twelve lead ECG and TMT ECG signal images (raw and filtered) (figure11b) as well as single-lead ECG and TMT ECG signal images extracted from the twelve lead signal images (raw, filtered) (figure11a).

In the developed prediction system, ECG and TMT ECG signal images of CAD and normal patients serve as input. It comprises of 552 twelve lead signal images and 6,624 extracted single lead signal images. 85% of the dataset is used for training, 10% for validation, and the remaining 5% for testing. The classification technique is developed based on two concepts: one with the consideration of the raw signal images immediately derived from the scanned ECG signal images, and the other one making use of filtered images, i.e., the resultant image after the pre-processing stage.



11(a)



11(b)

Figure 11(a) Flow chart of single lead prediction model (b) Flow chart of twelve lead prediction model.

The algorithm is developed to analyze the full behavior of cardiac disease under single lead and twelve lead conditions. The accuracy and computation loss of the proposed model was compared to a well-known pre-trained algorithm (VGG16, MobileNet, Inception, ResNet, and Efficient-Net) in the field of image classification using the transfer learning methods. The implementation of these pre-trained algorithms with the help of the transfer learning method for present data is discussed as follows and compared with the proposed implementation.

Transfer learning of VGG16

VGG16 is made up of five convolution layer blocks which are then linked to a multi-layer perceptron (MLP) classifier. The first three convolution layer blocks of VGG16 are not altered during transfer learning adaptation, as they were previously trained on the ImageNet dataset. The fourth and fifth blocks of the convolution are trained based on the current dataset, and this process is known as fine-tuning. This is because the model architecture allows the model to adjust the weights relevant to the current dataset. The fourth and fifth layers of the convolutional block are encoded with generic and reusable features, whereas the first three layers are encoded with specialized, trained dataset features. As a result of the changes to the fourth and fifth convolutional blocks, are learnt changes of features which are present in the current dataset.

The last convolution block is connected to three layers of a multi-layer perceptron, the first two of which are hidden layers and the third one is the output layer. Each of the first two hidden layers has 128 and 64 nodes respectively using a rectified linear unit (ReLU) as the activation function. The hidden layers are followed by dropout layers, which remove randomly 40% of the parameters. The output layer is made up of a single node with a sigmoid activation function that classifies data into any one of the two classes.

The Adam optimizer was used to train this model architecture, with a learning rate of 0.001. With standard split methodology, all datasets (training, validation, and testing) are flown to the model as per the defined batch size. In case of poor performance in validation for two consecutive epochs, the model architecture is programmed to reduce the learning rate by a factor of 0.5 and to cease training the model for future epochs if the validation loss does not improve for the next 5 epochs.

Transfer learning of MobileNet

During the implementation of the MobileNet model, the classification layer parameter is determined by the very last layer before the flattening process. This layer response will vary based on changes in the upper layer parameter. It is less important to change than the bottom layer since it preserves feature parameters linked to picture relevance rather than image generality. The frozen convolutional layer is considered as a base model for the feature extraction process. These feature vector values are converted into actual predictions, with an application of the global average pooling method. At the end of the process, this will transform feature vectors into 1280 element vectors.

Then, to forecast the existence of the disease, these vectors are connected to dense layers consisting of 512 neurons with ReLU activation function and an output layer consisting single neuron with sigmoid activation function respectively. The model's performance is assessed by a binary cross-entropy loss function and an Adam optimizer, and the outcomes are measured in terms of accuracy and loss function values with the help of previously defined trainable parameters and conditions.

Transfer learning of Inception

The 42 layers in the Inception model render it as a deep neural network for classification, and the performance of a class in Inception is primarily determined by the layer before the flattened layer. The initial learning technique is identical to MobileNet and both networks are varied only in terms of considering the parameter values. During feature extraction, the weights of the convolution layer are frozen and used to transform into real prediction, with the help of the element vector (18432) parameter, extracted from the feature vector using the global average pooling method. These element vectors are connected to the output layer of a single neuron with a sigmoid activation function, followed by a dense layer (512 neurons) having a ReLU activation function with a 40% dropout. The trainable parameters (batch size, learning rate, etc.) are considered as same as the proposed network condition.

Transfer learning of ResNet

The ResNet model is built using dimensional convolutional layers with three different types of filters. The first and third filters have 1x1 kernel sizes, while the second filter has a 3x3 kernel size. All three filters have the same stride. The residual blocks have three main stages. Except for the first stage, which has a 2x2 maximum pooling layer after the initial Conv2d layer, Batch normalization is applied between two subsequent Conv2d layers having ReLU activation function. The output of each stage is combined with original data and is passed through the ReLU activation function before moving to the next stage.

A 2X2 average pooling layer's output is connected to two dense layers together with the output of third stage, the first of which has 4096 neurons and the second of which has 2048 neurons. During transfer learning, additional three layers are mounted on ResNet's final layer. The first two layers of the three dense layers with 1024 and 512 neurons respectively are coupled to the ReLU activation function. The third one belongs to the output layer which has a single neuron with a sigmoid activation function, followed by a dropout layer of 40%, which will help to identify and classify the disease. To find the optimal model during classification, the model performance evaluation is carried out using the Adam optimizer and binary cross-entropy loss function with the help of defined trainable parameter values.

Transfer learning of EfficientNet

In general, any deep neural network is constructed with the goal of improving model performance, which leads to an increase in the number of units or layers. However, this method may or may not improve the performance. Considering this, the EfficientNet aids in the provision of an effective compound scaling strategy (which scales all dimensions, i.e., depth/width/resolution) for increasing model size in order to obtain maximum accuracy.

The study covers only the optimum method (EfficientNet-B0) and its application to the current data. EfficientNet model is a pre-trained model that uses an image with a size of (224, 224). Consideration of the feature distribution value of the image depends on all color channels (RGB) without normalizing. The EfficientNet pre-trained model was originally trained with ImageNet. These weights are considered for training present data to extract current features. Then these features are fed into fully connected layers having 512 neurons with ReLU activation function. These are then connected to the output layer with one neuron having a sigmoid activation function to classify the CAD and normal patient ECG's signals. The binary cross-entropy loss function and Adam optimizers are used to evaluate the performance of two classes with the help of standard trainable parameters.

Proposed classification model

The model which designed for CAD prediction is based on the effective factors that are considered in pre-trained models to improve model accuracy (i.e. effective depth, convolutional layer for feature extraction, and feature parameter selections in layers). Based on this information, the designed architecture uses 5 convolutional layer blocks (64, 32, 32, 32, and 128 neurons) with a kernel size of 5x5 along with a ReLU activation function. The output of each convolution layer is processed through a max-pooling layer with a size of 2x2. The layer-by-layer optimization is achieved by avoiding overfitting with the application of the dropout layer after the convolution layer, followed by the max-pooling layer. The flattened output of convolutions is considered as input to a fully connected layer with 128 neurons with a 40% dropout.

The fully connected layer is designed with ReLU activation function. It is connected to the output layer of a single neuron to represent one of the classes using the sigmoid activation function. The model architecture is trained using the Adam optimizer with a learning rate of 0.001 with consideration of small parameter values (batch size = 128, epochs, callbacks, etc.). The developed model architecture is shown in the figure 13.

The proposed model and pre-trained models are subjected to two types of datasets (i.e image data with an image size of 150 x 150 pixels). The first type of data is twelve lead dataset which consists of 512 patients' signal image data including normal and CAD patients corresponding to the state of rest and exercised condition. The second type is a similar dataset but is related to single lead data (of 1-sec durational data) totaling to 6,624 signal images.

The performance of the proposed convolutional based deep neural network is compared with pre-trained networks. Pre-trained models use the weights learnt from previous datasets (Imagenet) to be applied to the current data set to achieve the desired accuracy. During the development of the proposed deep neural network condition, weights are generated over the dataset which is imported as current data and predict the disease based on those weights. The standard protocol of data segregation is considered for both single and multi-lead data i.e. 85% for training, 10% for validation, and 5% for testing.

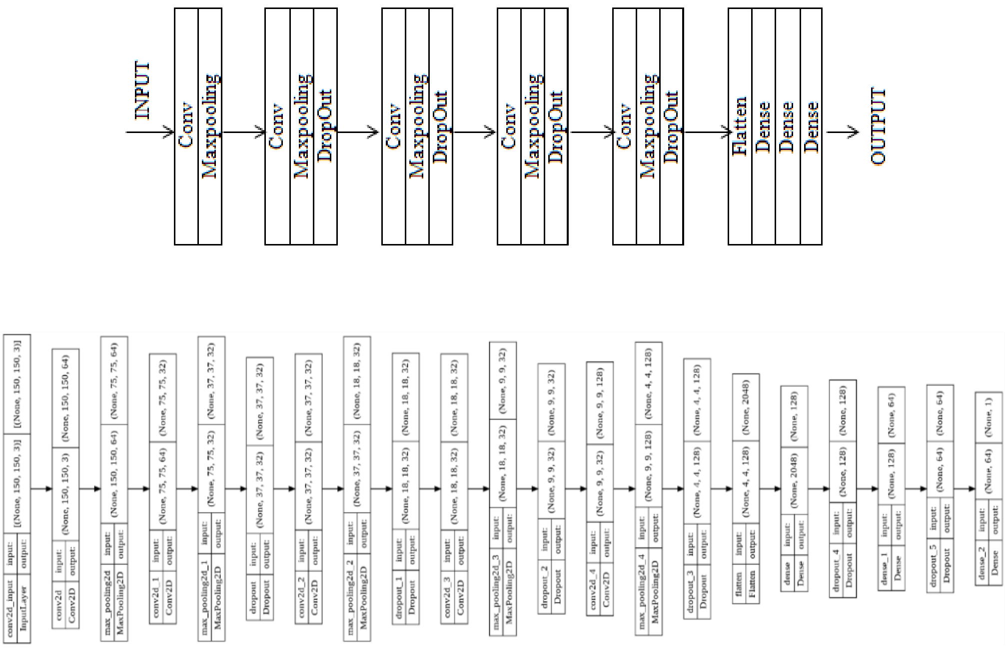


Figure 12: Layer details of developed network

Result and Discussions

The analyses is carried out for developed and pre-trained algorithms by using single lead and twelve lead data with consideration of normal ECG and TMT ECG under raw signal image conditions and filtered signal images which are obtained through image pre-processing. These algorithms are developed in python programming, with the support of a graphical processing unit (GPU) to reduce the computation time. The developed algorithm back-ended with Tensorflow helps to optimize the network. The data which are considered for analysis are twelve lead data (552 image samples), and single lead data (6,624 image samples) of patients which includes normal ECGs and exercised ECGs. These data are fed into 6 types of algorithms, five are pre-trained (transfer learnt) and the sixth is the developed model. The performance of the developed model is evaluated and compared based on the accuracy, loss function, ROC value, and confusion matrix.

Similar trainable parameters (batch size, learning rate, optimizers, and loss functions) are considered for all six algorithms. The batch size considered for the training algorithm is 128 and the learning rate is defined as 0.001 with consideration of the Adam optimizer and binary cross-entropy loss function. These algorithms are trained with an early stop condition if the performance does not improve (Validation loss) after 5 successful epochs. The accuracy of the model throughout training, validation, and testing for raw and filtered single-lead and twelve –lead ECG signal images are as follows.

Analysis of Single Lead

The single lead raw ECG signal image performance evaluation is shown in Table 1, it presents the accuracy and loss function of the developed CNN model in comparison to other models.

Table 1: Comparison of Transfer learned and developed models with raw data for single lead signal images

Model	Training		Validation		Testing	
	accuracy	loss	accuracy	loss	accuracy	loss
VGG16	90.20%	0.25	86.10%	0.30	89.16%	0.24
Inception	76.79%	0.45	77.05%	0.47	81.02%	0.40
Mobile net	89.57%	0.23	85.62%	0.31	89.16%	0.27
ResNet	57.38%	0.64	56.63%	0.64	57.53%	0.66
Efficient Net	73.85%	0.52	75.69%	0.49	79.82%	0.45
Developed CNN	77.74%	0.48	76.95%	0.48	78.13%	0.47

Table 2: Comparison of Transfer learned and developed models with filtered data for single lead signal images

Model	Training		Validation		Testing	
	accuracy	loss	accuracy	loss	accuracy	loss
VGG16	88.16%	0.27	85.94%	0.33	84.34%	0.34

Inception	86.73%	0.31	84.75%	0.37	87.05%	0.35
Mobile netv2	90.58%	0.23	86.10%	0.32	87.95%	0.27
RestNet	84.5%	0.35	82.4%	0.39	83.1%	0.41
Efficient Net	84.32%	0.34	86.18%	0.32	87.95%	0.30
Developed CNN	93.22%	0.17	92.7%	0.19	93.9%	0.21

The developed network with raw ECG signal image conditions exhibits poor accuracy due to insufficient feature parameters availability for prediction due to the presense of noise. This can be overcome with a filtered ECG signal image as shown in the Figure 13.

The filtered signal images are obtained by the pre-processing method and are used to train all six models. In this case, the developed CNN model outperforms all other pre-trained models, in terms of accuracy and loss. The developed model accuracy increased to 93.2% during training and 93.9% during testing when filtered images were used instead of the raw image, making it more suitable for implementation as a predictive system.

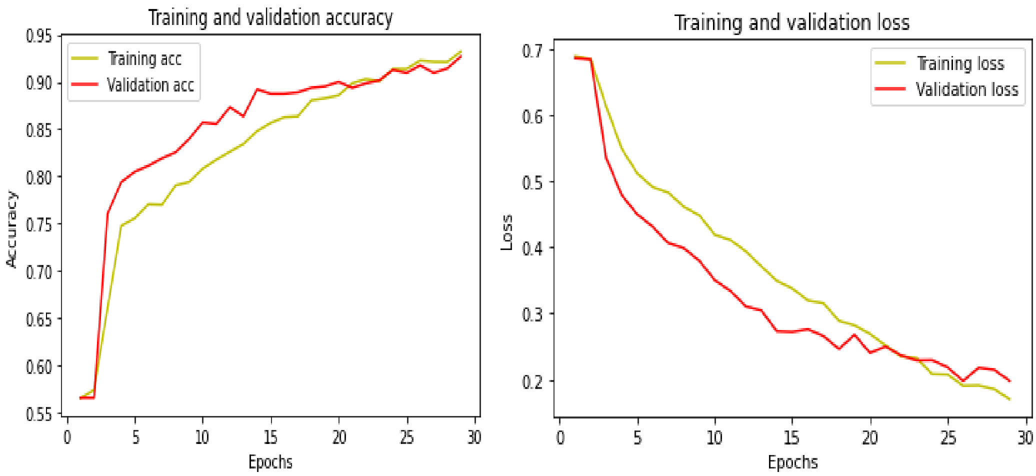
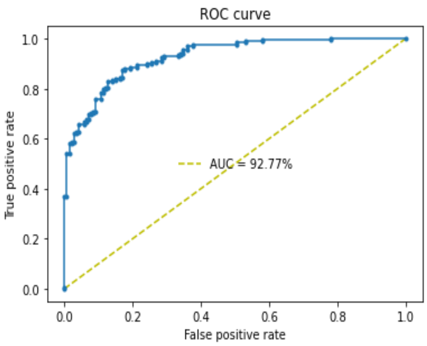


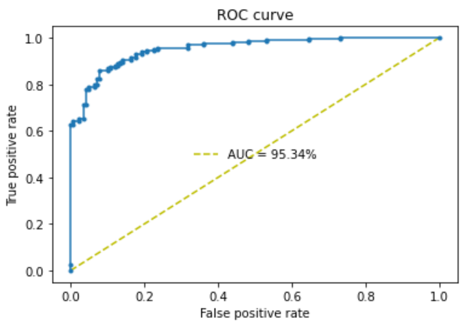
Figure 13: (a) Accuracy plot of developed network and (b) Validation loss of developed network

From the table 2 it is observed that MobileNet and VGG16 are bit closer to the performance of developed CNN model. Even though they are closer, these two pre-trained models are complex in nature compared to the developed model in terms of number of layers used (MobileNet = 53 and VGG16=16) and hence require more computational time for analysis. In the developed CNN model the number of layers used are 14, for the same or better accuracy and lesser computational time.

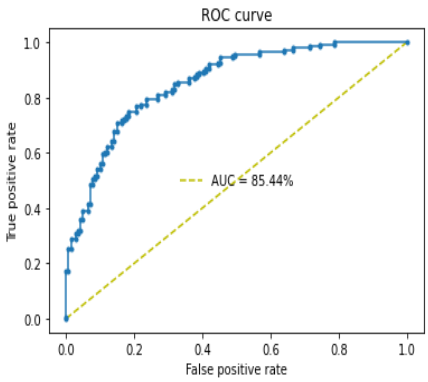
The models are evaluated by considering the testing (unseen) samples i.e., 5% (190 CAD and 142 NOCAD) in terms of the confusion matrix and ROC (Receiver Operating Characteristics) curve. The plot of the ROC curve for filtered single-lead ECGs and TMT-ECG with all conditions (six algorithms) that are considered for prediction analysis is shown in the figures 14a-14f. In the plot if the ROC curve is tend towards the upper left corner, then it reflects its effective performance in true positive classification of the model (Effective prediction of CAD and NOCAD images). The developed model has a very good ROC plot (Figure 14f), indicating that it has excellent binary classification diagnosis capability.



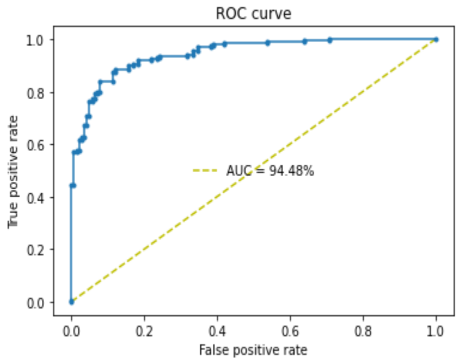
(a) ROC of VGG16



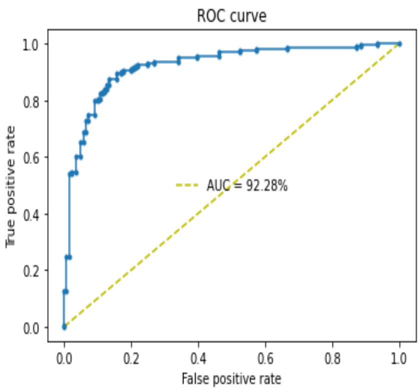
(b) ROC of MobileNet V2



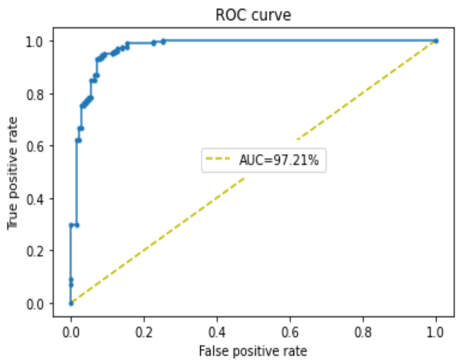
(c) ROC of ResNet 50



(d) ROC of EfficientNet



(e) ROC of Inception

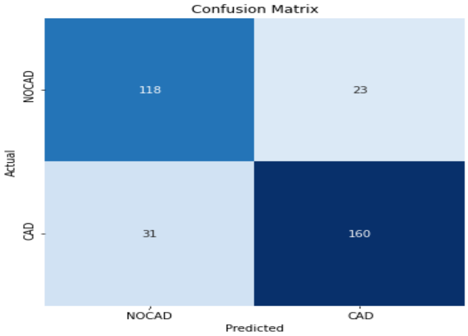


(f) ROC of developed model

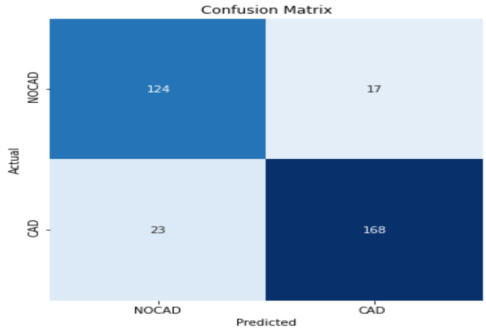
Figure 14 (a-f): Receiver Operating Characteristics (ROC) plot of transferred learning model and developed model.

Along with ROC, the confusion matrix (figure 15a-15f)) shows the number of image data lying on the True positive, True negative, False positive, and False-negative columns. Figures (15(a-f)) represent the percentage of filtered single-lead

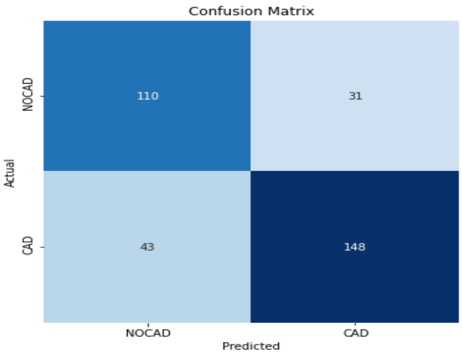
ECG signal images that were successfully classified in the confusion matrix. Out of 142 NOCAD images, the developed model achieved a high true positive classification rate. 132 images are successfully classified, while 177 CAD images are correctly classified against 190 images. The computational and analysis duration are significantly reduced because the network is not as deep as compared to other pre-trained algorithms.



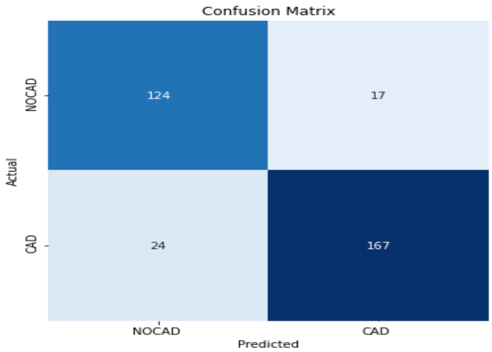
(a) Confusion matrix of VGG16



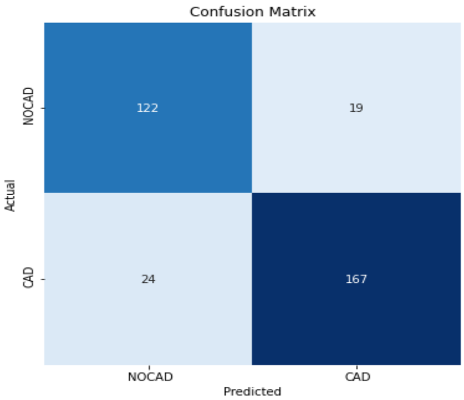
(b) Confusion matrix of MobileNet



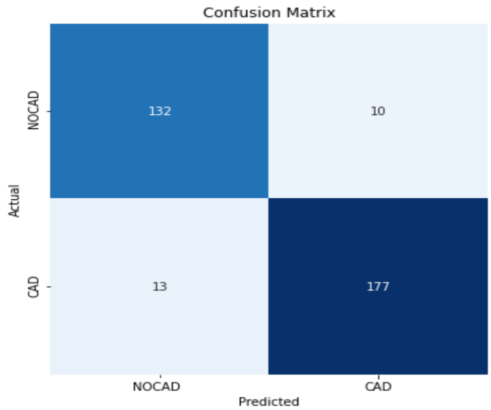
(c) Confusion matrix of ResNet50



(d) Confusion matrix of EfficientNet



(e) confusion matrix of Inception



(f) confusion matrix of Proposed model

Figure 15 (a-f): Confusion matrix plot of transferred learning model and developed model

For each epoch, the model classification accuracy score and loss score for testing and validation sets are examined. The basic idea behind having a loss score in deep network learning is, to use it as a feedback signal to alter the model's weights in order to reduce the loss score in the following train epoch. The test set (5%) is essential to know the model's generalizability about new and unknown data. Over-fitting occurs when a model achieves a high accuracy score in the training set but performs poorly in the validation set. This occurs when the model over-optimizes in its learning phase of the training image samples. This can be mitigated by tuning a network that improves model accuracy during training and validation by reducing loss function.

The mathematical representation of classification accuracy equation (2) is as follows:

$$Classification\ accuracy = \frac{correctly\ predicted\ samples}{total\ number\ of\ samples} \qquad (2)$$

In addition to classification accuracy, the model is evaluated with in terms of precision, recall, and F1 score. The precision, recall, and F1-score are derived using the confusion matrix. These parameter values provide a visual representation of the algorithms' evaluation. These parameters are calculated from all the pre-trained and developed models. Equations 3 to 5 mathematical definition of precision, recall, and F1 score respectively.

The accuracy and recall functions [28] are represented as follows:

$$precision = \frac{TP}{(TP+FP)} \qquad (3)$$

$$Recall = \frac{TP}{(TP+FN)} \qquad (4)$$

Where TP = True Positive, TN=True Negative, FP = False Positive, FN = False Negative.

The precision score reveals how many of the samples, the model predicted correctly as positive class and the recall score provides the information related to how many of the truly positive samples, the model predicted correctly as positive. The F1 measure score is frequently employed in conjunction with accuracy and recall scores since it functions as a harmonic mean and provides a more accurate and balanced score indicator [37].

Mathematically F1 score is calculated as follows:

$$F_1\ Score = \frac{2\ X\ Precision\ X\ Recall}{Precision+Recall} \qquad (5)$$

The accuracy score and confusion matrix performance is used to determine whether a prediction model is effective in classifying CAD disease based on ECG or TMT-ECG signal images. Table 3 shows the filtered single lead ECG images' precision, recall, and F1- Score values for CAD and NOCAD conditions.

Table-3: Precision, Recall And F1 Score of transfer learned and developed a network for single lead signal image data

Model	Precision		Recall		F1-score	
	NOCAD	CAD	NOCAD	CAD	NOCAD	CAD
VGG16	79	87	84	84	81	86
MobileNet V2	84	91	88	88	86	89
Inception V3	84	90	87	87	85	89
ResNet 50	72	83	78	77	75	80
Developed CNN	91	95	93	93	92	94

The precision, which specifies how many samples of images that the model predicts, belong to the real class was around 95 percent for CAD and 91 percent for NOCAD. The recall reflects how many real samples of images were properly predicted by the algorithm (model), and the score obtained for CAD and NOCAD images is 93 percent. Similarly, the F1-Score functions as a harmonic mean of precision and recall, and the developed model achieves a very good and acceptable score when compared to other pre-trained models (i.e., 94 for CAD and 92 for NOCAD images).

Analysis of Twelve Lead

The twelve lead raw ECG signal image performance evaluation is shown in Table 4, it presents the accuracy and loss function of the developed CNN model in comparison to other models.The developed model for raw images condition exhibits poor performance which can overcome with model trained using filtered images. The filtered images are derived from the raw image using a defined image pre-processing methodology. These filtered signal images are considered as input to the developed algorithm, results better than the pre-trained algorithm (94.03 percent) (Table-4).

Table-4: Comparison of Transfer learned and developed models' with raw data for twelve lead signal images

Model	Training		Validation		Testing	
	accuracy	loss	accuracy	loss	accuracy	loss
VGG16	92.99%	0.17	86.79%	0.35	78.87%	0.40
Inception V3	87.03%	0.07	88.68%	0.33	82.14%	0.53
Mobile netv2	93.66%	0.08	90.57%	0.28	85.71%	0.29
ResNet 50	57.11%	0.68	60.38%	0.67	53.57%	0.72
Efficient Net	89.08%	0.23	84.91%	0.29	85.71%	0.31
Developed CNN	76.90%	0.48	70.38%	0.48	73.57%	0.49

Table-5: Comparison of Transfer learned and developed models' with filtered data for twelve lead signal images

Model	Training		Validation		Testing	
	accuracy	loss	accuracy	loss	accuracy	loss

VGG16	90.87%	0.20	88.68%	0.21	89.2%	0.36
Inception	85.77%	0.46	88.68%	0.55	92.86%	0.37
Mobile netv2	93.97%	0.12	93.23%	0.22	89.28%	0.32
RestNet	57.11%	0.69	60.38%	0.69	53.57%	0.67
Efficient Net	86.62%	0.37	90.57%	0.23	85.7%	0.37
Developed CNN	94.03%	0.17	94.34%	0.21	100%	0.04

The filtered image (ECG& TMT ECG) condition, the accuracy plot, and the validation loss plot generated for the developed algorithm demonstrate good accuracy compared to pre-trained or transfer learning models. The correlation between training and validation accuracy is shown in the figure (16a) with respect to epochs. It also shows the relationship between validation loss, during the time of training and validation as shown in figure 16 (b) with respect to epochs.

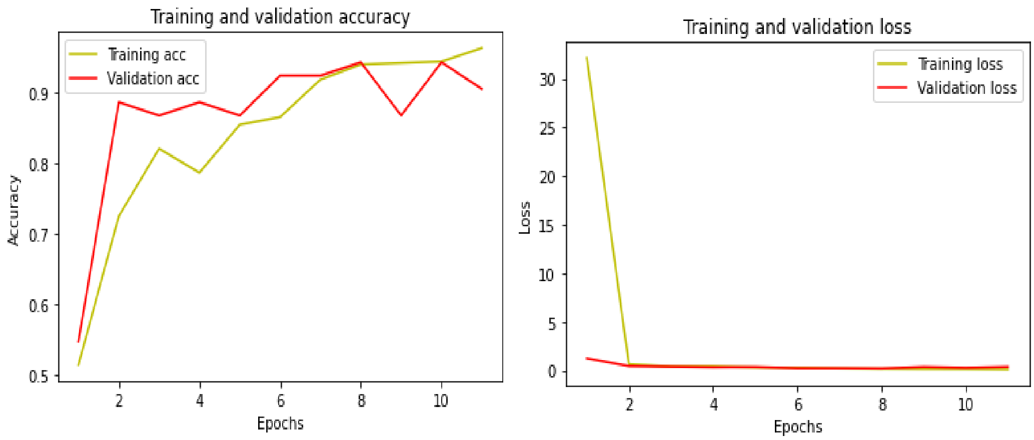
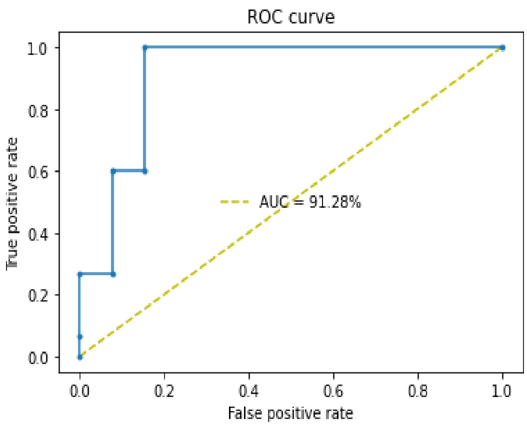
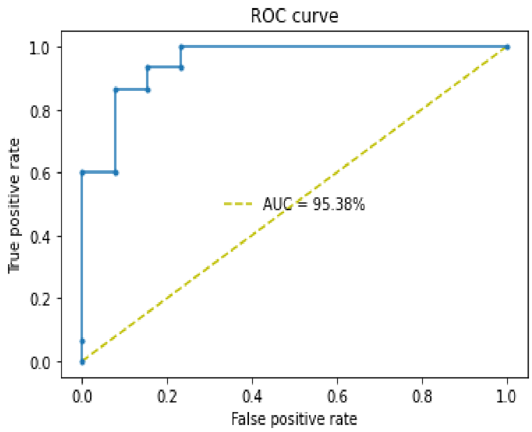


Figure 16: (a) Accuracy plot of the developed model and (b) Validation loss plot of the developed model for 12 lead signal images

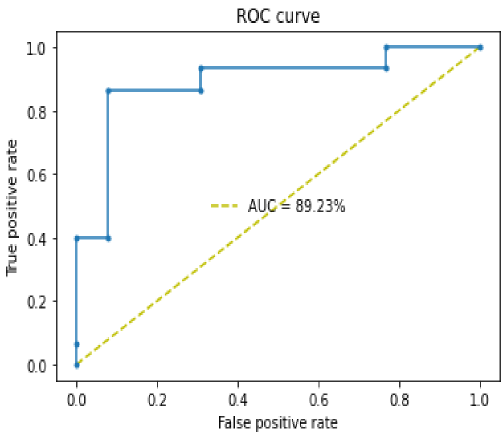
The algorithms which are developed and transfer learned are further evaluated based on the ROC plot and confusion matrix similar to the analysis of a single lead image condition. The figures (17 a – 17f) show the performance of six algorithms (five pre-trained transfer learned and one developed) in terms of the ROC curve that tend towards the upper left corner relates to the true positive rate of prediction. The ROC plot of the developed algorithm demonstrates a good true positive rate of 100 percent for the categorization of CAD and NOCAD images.



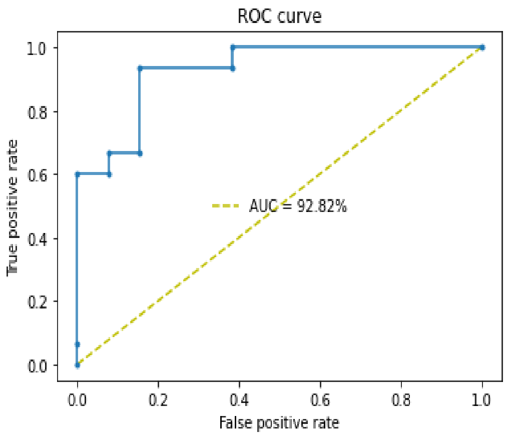
(a) ROC of VGG16



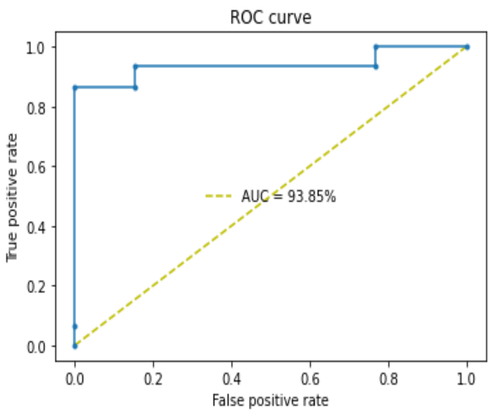
(b) ROC of MobileNet V2



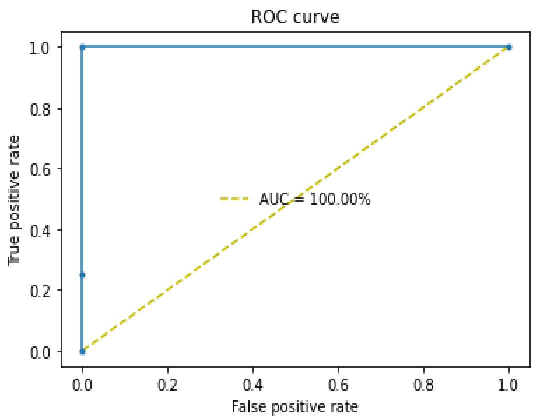
(c) ROC of ResNet 50



(d) ROC of EfficientNet 50



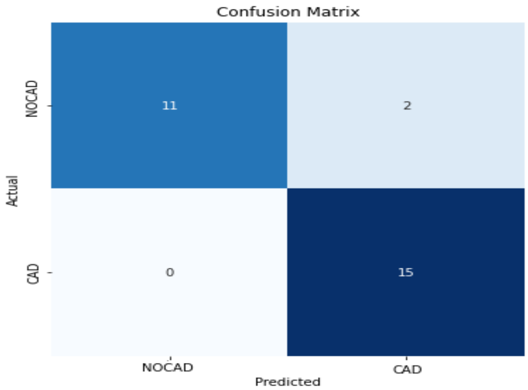
(e) ROC of Inception

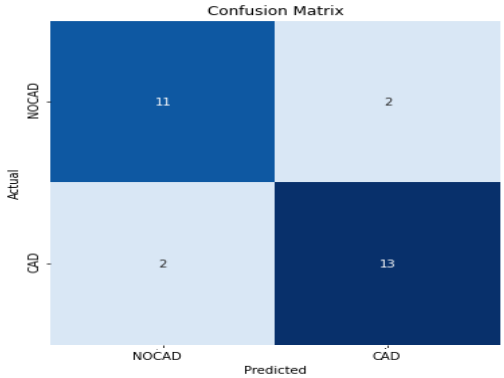


11.a) ROC of proposed model

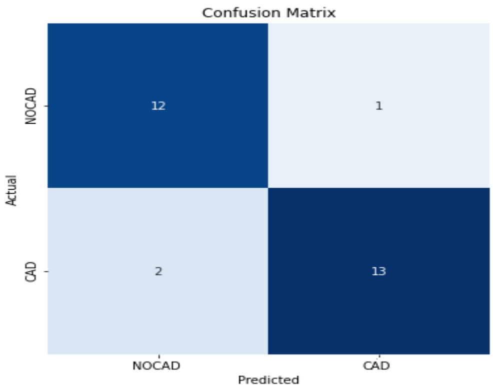
Figure 17 (a-f): Receiver Operating Characteristics (ROC) plot of transferred learning model and developed model for twelve lead signal images.

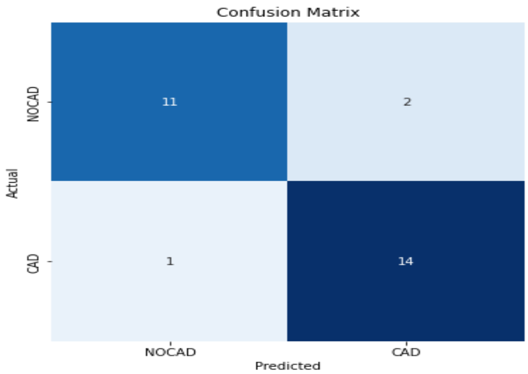
The confusion matrix helps to visualize the quantity of data which are classified for the same class and opponent class. Figures 18(a-f) shows the confusion matrix for the transfer learned algorithms and developed algorithm for test images of 12 lead ECG signals. The confusion matrix parameters (True Positive, True Negative, False Positive, and False Negative), indicate the efficiency of the developed algorithm to classify CAD and NOCAD. Under the filtered 12 lead signal image condition the developed algorithm shows a clear classification of test images for CAD and NOCAD classes (100 percent accuracy of test images).



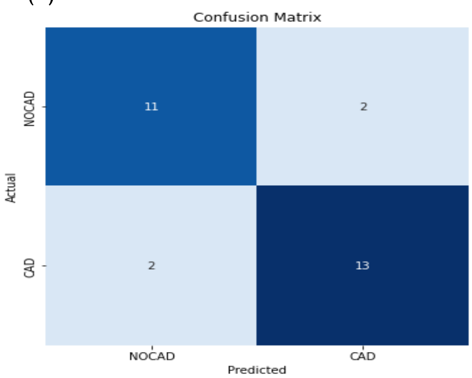


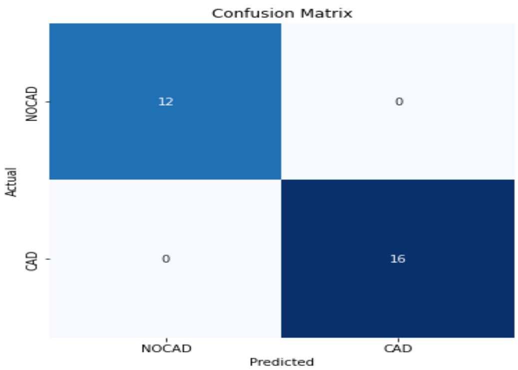
(a) Confusion matrix of VGG16 (b) Confusion matrix of MobileNetV2





(c) Confusion matrix of ResNet (d) Confusion matrix of Efficient Net





(e) Confusion matrix of Inception (f) Confusion matrix of developed model

Figure 18 (a-f): Confusion matrix plot of transferred learning model and developed model.

The parameters precision, recall, and F1-score which are derived from the confusion matrix are used to further evaluate all six algorithms. Table -6 represents the precision, recall, and F1-score values of the developed algorithm and pre-trained algorithms for filtered 12 lead ECG and TMT-ECG signal image conditions. The developed model shows very good and acceptable results throughout all parameters under test image conditions. Hence the developed model can be implemented as a predictive tool in the medical field to identify the existence of coronary artery disease patients.

Table-6: Precision, Recall and F1 Score of transfer learned and developed network for 12 lead signal image data

Model	Precision		Recall		F1-score	
	CAD	NOCAD	CAD	NOCAD	CAD	NOCAD
VGG16	88%	100%	100%	85%	94%	92%
MobileNet	87%	85%	87%	85%	87%	85%
Inception	87%	85%	87%	85%	87%	85%
ResNet	93%	86%	87%	92%	90%	89%
Efficient Net	88%	92%	93%	85%	90%	88%
Developed CNN	100%	100%	100%	100%	100%	100%

This model can be extended to include further more examination results of ECG/TMT ECG image dataset in order to strengthen it as a full-fledged Coronary artery disease prediction tool. However, this will support the doctors practicing general medical profession in a rural area (remote places) to identify the severity of the CAD disease. The developed model can also help doctors to take a second opinion when they come across crucial CAD patients. To support this scenario a graphical user interface (GUI) is developed using the proposed CNN model (Figure16 home page). In the developed application GUI the prediction is taking into account of trained weights of the developed CNN model with consideration of single lead and twelve lead ECG and TMT ECG signal images. In a developed GUI, the medical expert needs to upload the images of ECG and TMT ECG records obtained during the medical examination. There is an option provided for the medical expert to select whether the medical examination is performed with the help of single lead ECG images or 12 lead ECG images (ECG & TMT ECG).

Figure 19: GUI home page of the prediction model

The developed application takes into consideration all the steps (pre-processing, filtering, and prediction) discussed in the earlier sections of the paper. The output of the GUI is based on the results obtained by developed CNN model predictions, which indicate the presence of CAD or NOCAD for the uploaded image of the patient. This developed CNN model will support the medical professionals by strengthening their diagnosis related to heart diseases.

Conclusions

The efficient predictive system supports the doctors to diagnose CAD in the early stage. To develop this predictive system a sequential deep learning model is developed based on CNN. The developed CNN model effectively classifies the disease over single lead and multi-lead (12 lead) ECG and TMT ECG signal image datasets. The evaluation of classification of image dataset is executed based on raw image and filtered image dataset (which are achieved from pre-processing methodology). Since it is a signal image classification, the developed algorithm results are compared with well-known transfer learned algorithms (VGG16, MobileNet, Inception, ResNet, EfficientNet) in terms of accuracy, confusion matrix, and ROC. The developed algorithm predicted CAD with 93.5% accuracy for a single lead and 94.5% accuracy for twelve lead ECG and TMT ECG signal images. It also showed better accuracy with less no of layers compared to well-known transfer learned algorithms and reducing computation time. The algorithm-based GUI supports the healthcare experts in rural areas to diagnose CAD with a single lead and twelve lead ECG signal images effectively.

References

1. Abas, M.A.H.; Ismail, N.; Yassin, A.I.M.; Taib, M.N. VGG16 for plant image classification with transfer learning and data augmentation. *Int. J. Eng. Technol.* 2018, *7*, 90–94, doi:10.14419/ijet.v7i4.11.20781.
2. Alizadehsani, R.; Roshanzamir, M.; Abdar, M.; Beykikhoshk, A.; Khosravi, A.; Panahiazar, M.; Koohestani, A.; Khozeimeh, F.; Nahavandi, S.; Sarrafzadegan, N. A database for using machine learning and data mining techniques for coronary artery disease diagnosis. *Sci. Data* 2019, *6*, 1–13, doi:10.1038/s41597-019-0206-3.
3. Al-Khatatneh, A.; Pitchay, S.A.; Al-Qudah, M. A Review of Skew Detection Techniques for Document. *Proc. - UKSim-AMSS 17th Int. Conf. Comput. Model. Simulation, UKSim 2015* 2016, 316–321, doi:10.1109/UKSim.2015.73.
4. Alzubaidi, L.; Zhang, J.; Humaidi, A.J.; Al-Dujaili, A.; Duan, Y.; Al-Shamma, O.; Santamaría, J.; Fadhel, M.A.; Al-Amidie, M.; Farhan, L. *Review of deep learning: concepts, CNN architectures, challenges, applications, future directions*; 2021; Vol. 8; ISBN 4053702100444.
5. Andreotti, F.; Carr, O.; Pimentel, M.A.F.; Mahdi, A.; De Vos, M. Comparing feature-based classifiers and convolutional neural networks to detect arrhythmia from short segments of ECG. *Comput. Cardiol. (2010).* 2017, *44*, 1–4, doi:10.22489/CinC.2017.360-239.
6. Arafat, S.; Dohrmann, M.; Skubic, M. Classification of coronary artery disease stress ECGs using uncertainty modeling. *2005 ICSC Congr. Comput. Intell. Methods Appl.* 2005, *2005*, 10–13, doi:10.1109/cima.2005.1662362.
7. Baek, Y.; Lee, B.; Han, D.; Yun, S.; Lee, H. Character region awareness for

text detection. *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.* 2019, *2019-June*, 9357–9366, doi:10.1109/CVPR.2019.00959.

8. Bertalmío, M.; Bertozzi, A.L.; Sapiro, G. Navier-Stokes, fluid dynamics, and image and video inpainting. *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.* 2001, *1*, doi:10.1109/cvpr.2001.990497.
9. Clifford, G.D.; Liu, C.; Moody, B.; Lehman, L.H.; Silva, I.; Li, Q.; Johnson, A.E.; Mark, R.G. AF classification from a short single lead ECG recording: The PhysioNet/computing in cardiology challenge 2017. *Comput. Cardiol. (2010).* 2017, *44*, 1–4, doi:10.22489/CinC.2017.065-469.
10. Ebrahimzadeh, E.; Pooyan, M. Early detection of sudden cardiac death by using classical linear techniques and time-frequency methods on electrocardiogram signals. *J. Biomed. Sci. Eng.* 2011, *04*, 699–706, doi:10.4236/jbise.2011.411087.
11. Ghiasi, S.; Abdollahpur, M.; Madani, N.; Kiani, K.; Ghaffari, A. Atrial fibrillation detection using feature based algorithm and deep convolutional neural network. *Comput. Cardiol. (2010).* 2017, *44*, 1–4, doi:10.22489/CinC.2017.159-327.
12. Jahmunah, V.; Oh, S.L.; Wei, J.K.E.; Ciaccio, E.J.; Chua, K.; San, T.R.; Acharya, U.R. Computer-aided diagnosis of congestive heart failure using ECG signals – A review. *Phys. Medica* 2019, *62*, 95–104, doi:10.1016/j.ejmp.2019.05.004.
13. Jian, J.Z.; Ger, T.R.; Lai, H.H.; Ku, C.M.; Chen, C.A.; Abu, P.A.R.; Chen, S.L. Detection of myocardial infarction using ecg and multi-scale feature concatenate. *Sensors* 2021, *21*, 1–17, doi:10.3390/s21051906.
14. jonathan C. Brown et.al. Risk factors for coronary artery disease. *Recenti Prog. Med.* 2022, *93*, 1–17.
15. kaisJameel, S.; R. Manza, R. Color image segmentation using wavelet. *Int. J. Appl. Inf. Syst.* 2012, *1*, 1–4, doi:10.5120/ijais12-450134.
16. Li, S.; Wang, L.; Li, J.; Yao, Y. Image Classification Algorithm Based on Improved AlexNet. *J. Phys. Conf. Ser.* 2021, *1813*, doi:10.1088/1742-6596/1813/1/012051.
17. Loganathan, P.; Karthikeyan, R. Residual Neural Network (ResNet) Based Plant Leaf Disease Detection and Classification. 2021, *12*, 1395–1401.
18. Manda, Y.R.; Baradhi, K.M. Cardiac Catheterization, Risks and Complications. *StatPearls* 2019, 1–6.
19. Martis, R.J.; Acharya, U.R.; Adeli, H. Current methods in electrocardiogram characterization. *Comput. Biol. Med.* 2014, *48*, 133–149, doi:10.1016/j.compbiomed.2014.02.012.
20. Mehrotra, R.; Ansari, M.A.; Agrawal, R.; Anand, R.S. A Transfer Learning approach for AI-based classification of brain tumors. *Mach. Learn. with Appl.* 2020, *2*, 100003, doi:10.1016/j.mlwa.2020.100003.
21. Moody, G.B. Spontaneous termination of atrial fibrillation: A challenge from PhysioNet and Computers in Cardiology 2004. *Comput. Cardiol.* 2004, *31*, 101–104, doi:10.1109/cic.2004.1442881.
22. Moody, G.B.; Mark, R.G. The impact of the MIT-BIH arrhythmia database. *IEEE Eng. Med. Biol. Mag.* 2001, *20*, 45–50, doi:10.1109/51.932724.
23. Mukhopadhyay, P.; Chaudhuri, B.B. Author ' s Accepted Manuscript A Survey of Hough Transform. *Pattern Recognit.* 2014.
24. Oh, S.L.; Adam, M.; Tan, J.H.; Hagiwara, Y.; Sudarshan, V.K.; Koh, J.E.W.; Chua, K.C.; Chua, K.P.; Tan, R.S.; Ng, E.Y.K. Automated identification of

coronary artery disease from short-term 12 lead electrocardiogram signals by using wavelet packet decomposition and common spatial pattern techniques. *J. Mech. Med. Biol.* 2017, *17*, doi:10.1142/S0219519417400073.
25. Rafieian-Kopaei, M.; Setorki, M.; Doudi, M.; Baradaran, A.; Nasri, H. Atherosclerosis: Process, indicators, risk factors and new hopes. *Int. J. Prev. Med.* 2014, *5*, 927–946.
26. Raid, A..; Khedr, W..; El-dosuky, M..; Aoud, M. Image Restoration Based on Morphological Operations. *Int. J. Comput. Sci. Eng. Inf. Technol.* 2014, *4*, 9–21, doi:10.5121/ijcseit.2014.4302.
27. Sandler, M.; Howard, A.; Zhu, M.; Zhmoginov, A.; Chen, L.C. MobileNetV2: Inverted Residuals and Linear Bottlenecks. *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.* 2018, 4510–4520, doi:10.1109/CVPR.2018.00474.
28. Sharma, S.; Mehra, R. Conventional Machine Learning and Deep Learning Approach for Multi-Classification of Breast Cancer Histopathology Images—a Comparative Insight. *J. Digit. Imaging* 2020, doi:10.1007/s10278-019-00307-y.
29. Sokolova, M.; Lapalme, G. A systematic analysis of performance measures for classification tasks. *Inf. Process. Manag.* 2009, *45*, 427–437, doi:10.1016/j.ipm.2009.03.002.
30. Srivastava, R.K.; Greff, K.; Schmidhuber, J. Highway Networks. 2015.
31. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Health and treatment of diabetes mellitus. *International Journal of Health Sciences*, *5*(1), i-v. https://doi.org/10.53730/ijhs.v5n1.2864
32. Szegedy, C.; Liu, W.; Jia, Y.; Sermanet, P.; Reed, S.; Anguelov, D.; Erhan, D.; Vanhoucke, V.; Rabinovich, A. Going deeper with convolutions. *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.* 2015, *07-12-June*, 1–9, doi:10.1109/CVPR.2015.7298594.
33. Tan, M.; Le, Q. V. EfficientNet: Rethinking model scaling for convolutional neural networks. *36th Int. Conf. Mach. Learn. ICML 2019* 2019, *2019-June*, 10691–10700.
34. U.R., Acharya, sree, vinitha, swapna, et. al. Linear and nonlinear analysis of normal and CAD-affected heart rate signals. *Comput. Methods Programs Biomed.* 2014, *113*, 55–68, doi:https://doi.org/10.1016/j.cmpb.2013.08.017.
35. Vasudeva, S.T.; Rao, S.S.; Panambur, N.K.; Mahabala, C.; Dakappa, P.H.; Prasad, K. Diagnostic classification of undifferentiated fevers using artificial neural network. *AIP Conf. Proc.* 2020, *2236*, doi:10.1063/5.0007749.
36. Viliane Vilcant; Roman Zeltser . Treadmill Stress Testing. *StatPearls* 2022.
37. Zhu, R.; Wang, Y. Application of improved median filter on image processing. *J. Comput.* 2012, *7*, 838–841, doi:10.4304/jcp.7.4.838-841.
38. Zu Li, H.; Boulanger, P. A survey of heart anomaly detection using ambulatory electrocardiogram (ECG). *Sensors (Switzerland)* 2020, *20*, doi:10.3390/s20051461.