Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

Diagnosing Cardio Vascular Disease (CVD) using Generative Adversarial Network (GAN) in Retinal Fundus Images

T.K.Revathi[1], B.Sathiyabhama[2], S.Sankar[3]

[1,3]Assistant Professor, Department of CSE, Sona College of Technology, Salem
(revathi.tk@sonatech.ac.in, sankar.cse@sonatech.ac.in)
[2]Professor and Head, Department of CSE, Sona College of Technology, Salem (sathiyabhama@sonatech.ac.in)

ABSTRACT

In most developing countries cardiovascular diseases (CVDs) is one of the primary causes of mortality. In India, it is estimated that the disease prevalence is very high and one in 4 deaths happens due to CVD. There is no proper specific programmes have been addresses to control CVDs as like existing communicable diseases. The proposed work uses Retinal fundus images in identifying the potential risk factors causes CVD in terms micro structural changes happens in its blood vessels. Hypertensive Retinopathy and Cholesterol-Embolization Syndrome (CES) are the most adverse factors affect the heart function which leads to CVD. These two factors are exactly identified in optic-disc of retinal vasculature. Generative Adversarial Network (GAN) is uses as a deep learning model to synthesize the images with high resolution, which is used in predicting the severity level of the CVD. This work also uses an existing retraining ImageNet model for solving custom image classification tasks. It observes that the experimental results show that the prediction accuracy rate will be high when compared with other existing deep learning approaches. The proposed work diagnoses the prevalence rate of CVD effectively and gives solution to the medical practitioners to adhere proper treatment in avoiding adverse risk.
Keywords: cardiovascular diseases - Cholesterol-Embolization Syndrome - Hypertensive Retinopathy - Generative Adversarial Network

Introduction

Heart is one of the most important organs in the human body and is made up of two chambers called an atrium and ventricle which are divided by two halves. These two chambers play vital roles in pumping blood in and out of the heart and body. The malfunction happens in those chambers leads to heart disease or sometimes called as cardiac disease. It is must to detect the disease early it happens may prevent the mortality rate.
Machine Learning (ML) and deep learning are making the healthcare industry smarter. These influential subsets of Artificial Intelligence (AI) may impacts in many fields such as Disease prediction, Speech recognition which is done by voice assistants. Also these technologies are useful in creating personalized online shopping experiences and video classification [1][2]. Particularly Recurrent networks are used for object detection purposes [3] [4]. More importantly, scientists and researchers are using machine learning (ML) and deep learning (DL) to produce a number of smart solutions that can ultimately help in diagnosing and treating an illness in an effective manner. Almost all type of health images like CCTA, Magnetic Resonance Imaging (MRI) are computed effectively by deep learning technique [5][6][7]. These technologies are allowing the patients to get benefit to know about their health outcome in an improvised manner by analyzing the best forms of treatment for them. Various methods like bounded box in object detection, edge detection [8] in object identification improves the algorithm to work better for the outcome.

Literature Review

Cardio Vascular Disease

CVD is identified as one of the most leading deadly diseases in the world. It happens due to the plaque build-up inside the coronary artery wall. This becomes narrowing in the coronary artery lumen which limits the blood flow to the heart. Narrowing of the arteries is known as Stenosis. The entire blockage in the artery potentially leads the Myocardial Infarction (MI) commonly known as a heart attack [9]. There are different kind of diagnosis are available for predicting the disease [10]. These coronary plaques diffuse the fat content to the proximal side wall to the vessel and it causes the coronary inflammation. This kind of inflammation is the leading cause for heart attack.

Present biomarkers suitable for predicting the heart disease only after it happens. It is a challenging task to diagnose a heart attack as early as it happens. Recently, a new biomarker Fat Attenuation Index (FAI) proposed by

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

the medical practitioners of Centre of Research Excellence, British Heart Foundation for diagnosing future fatal heart attack many years before it happens [11]. It is crucial to detect and classify the coronary inflammation to prevent the heart attack as early as possible. Fat attenuation Index (FAI) is an imaging biomarker quantifies the inflamed coronary artery and is clinically obtained using non-invasive Coronary Computed Tomography Angiography (CCTA) test [11][12].

Preventing patients from future heart attack, they are advised to take further non-invasive tests. The coronary artery plaque can be classified into three categories. They are a calcified plaque, non-calcified plaque and mixed plaque based on its composition [13]. Formation of these plaques and its rupture leads to the acute coronary syndrome and it causes to the Myocardial Infarction (MI) or heart attack [11], [14]. Coronary artery Stenosis is narrowing of the arteries. Severe blockage of arteries may cause a heart attack [9]. Coronary artery calcium score (CACS) is a tool which plays a significant role in diagnosing coronary artery stenosis disease. The predictive value of CACS is used to find the presence and severity of Coronary Artery Disease (CAD) in patients. Although it does not exactly predicts all kinds of causes of the disease as well as the cardiac mortality.

Vascular inflammation in the arteries enables timely exploitation of measures to prevent future heart attacks. A new imaging biomarker called Fat Attenuation Index (FAI) around Coronary Artery is used to diagnose coronary inflammation and also it identifies individuals at risk of cardiac mortality. FAI captures fat attenuation of perivascular and it detects vascular inflammation at an early with routine Coronary Computed Tomography Angiography CCTA [13]. There are many invasive and non-invasive tests or procedures available to detect heart disease. Coronary Computed Tomography Angiography (CCTA) is a heart imaging tool that provides the details about the plaque information present in the coronary arteries [13], [15]. It is a sensitive and widely used diagnostic tool for the diagnosing coronary CAD [16]. The thickness of luminal plaque and the details of plaque composition were determined by CCTA. The vessels can also be diagnosed as like retinal fundus images, since both CCTA and Retinal images are vessel based structure [17], [18].

Analysis of coronary arterial vessel provides needed details about conditions of the blood flow and systemic level of the blood voltage [19]. Cardiologists can detect the sign of systemic vessel burden early it happens. From speed and voltage of blood flow cardiac threatening diseases such as CAD and Heart attack were also be found from abnormality in the coronary artery structures [19-20]. The noises have been eradicated using 3D artifacts removal technique [21] the arteries will be clear in finding the vessels in a clear manner. An adaptive block-matching 3D algorithm used for handling Low-dose Computed tomography images [22-23].

Coronary Artery diseases can also be predicted using retinal fundus risk factors [24-25]. Moreover the researchers no need to worry about the dataset limitation. Scientists can collect easily the retinal image based on that they can validate their model. To assist analysis, automatic artery segmentation method, especially from CCTA images, has been used widely for doing research. In ancient days, numerous computer visions based algorithms were deals about this problem from the perception of signal processing [26-27]. In this type of assumption the researchers have been followed to denoise the CCTA images from particular patterns for segmenting the vessels [28-29]. SVD based algorithm is also been proposed for the sparse representation of an image dataset [30]. Long-term recurrent convolutional network is being used for visual recognition of image data and semantic approaches also give better outcome to the image visualization [31].

Various heuristic methods such as line detection [32] [17] and feature extraction based hand-crafted methods were used in determining the disease [33-34]. However, more improved results were obtained, with the advance techniques of machine learning and from feature learning automation technique. For instance, the features of vessel automatically extracted using gradient boosting [35] and scientists anticipated to introduce Conditional Random Field (CRF). Their parameters are qualified from curvilinear structure segmentation of the data with the structured Support Vector Machine (SVM) [35].

In recent times, Convolutional Neural Network [36-37] has remarkable outcomes for several computer vision problems. Several literature surveys portray that CNNs has the better performance in doing the segmentation process of vessels in any body organs and even outstands to the ability of human specialists in multiple datasets [24-25], [38-39]. However, the segmented vessels of all these methods are rather unclear and suffer from tiny and faint tubes of the arteries. This happens because of the kernel function applied in the CNNs. The existing methodologies only depends on the pixel-wise kernel functions and also it compares model generated images with standard images.

This is not providing the desirable outcome since it cannot aggressively accommodate natural vessel structure that exist in CCTA images. In fact, the segmentation of coronary arteries can be considered as an image translation problem. From an input image, a segmented artery vessel map is generated. If the output images are inhibited to look like the doctors' annotation, then clear and sharp artery vessel maps can be attained from the proposed method of GAN.

Generative Adversarial Networks (GANs) is a special kind of framework which allows to create as rational output [40]. GANs contains two different networks namely discriminator and generator. The discriminator tries to differentiate standard images from the outputs which are generated through generator. The generator is responsible in producing realistic outputs. This cannot be done by the discriminator whereas the generator cannot differentiate the standard image from model generated image.

In this paper, a new methodology has been introduced to coronary artery segmentation with generative adversarial networks. The clear and sharp features of coronary artery vessels were extracted by the proposed method with fewer false positives compared to existing methods. It also achieves the state-of-the-art performance in the public dataset, namely, UCI Heart Disease Repository. The adversarial training improves the quality of the image segmentation. This is been done by training the generator and to extracting the identical coronary artery vessel maps from the maps annotated by doctors or human scientists.

Clinical Database Analysis

Clinical database contains patients heart related information which are used to identify factors that contribute to the heart attack prediction [41]. The knowledge discovery is used to identify the influence that helps in improving the quality and provides better to the patients care.

Differential diagnostic procedure [10] is a systematic diagnostic method. In this method condition based identification is used to find the presence of a disease entity where multiple alternatives are possible. The major complaint is examined with respect to the causal factors [42] and concurrent occurrences perceived by suitable disciplinary outlook. According to various theoretical paradigms, the presence of the disease is identifies and compared to known categories of any disease which the researcher encountered for diagnosis. This method may establish several algorithms to the process of elimination and also it is used to obtain the information minimizes the probabilities of candidate conditions. This is insignificant levels for the scientists who are working with the evidence such as symptoms, patient history, and medical knowledge.

Retinal images are one of the most significant tool to predict various cardiovascular risk factors. It is stated that rather numerical and ECG signals, the image data could be correlated directly with cardiovascular events [43].

Recently the use of deep learning helps in resulting the outcome for detecting age, patient’s gender information, systolic Blood Pressure (BP), diastolic BP and smoking habits from the fundus photographs. The AI based system [44] had equivalent Area under Curve (AuC) to the traditional risk calculators in predicting severe cardiovascular risks. The model developed seems to be effective imaging modality to assess the CVDs events.

In most developing countries CVDs is the principal causes of mortality. In India, as of 2016, the estimated prevalence of CVDs to be 54.5 million. Due to CVDs one in 4 deaths happens. CVDs have not been addressed properly under specific control programmes as like existing communicable diseases. Hypertension accounted for 80% of the CVDs events to be happened. It is clearly indicated that risk factor like systolic blood pressure and plasma cholesterol contributed to the surplus risk of CVD [45].

Indian Council of Medical Research (ICMR) estimates that, the count of hypertensive is expected to rise up to 214 million in 2025. So, this project wants to address these hypertensive risk factors appropriately. The retinal fundus is the potential biomarker to find the hypertensive periodically based on its micro structural changes. And also India needs priority action to highlight the knowledge of physicians, individuals and communities about the risk factors and make them to adherence the proper treatment to the patients. This paper produce the evidence based recommendation to emphasize physicians’ knowledge on treating patients. The improper follow up of bedside patients will cause the patients to revisit infinitely [45].

Methods

Proposed Work

An ensemble based framework of different neural network (NN) models for random sample aggregation is used to classify heart disease. The performance of the classification algorithms are improved by doing the data pre-processing step followed by features selection process. Various experiments have been conducted with unidirectional and bidirectional NN models. The results shows that an ensemble classifier with a CNN model had the best performance with improved accuracy and F1-score between 91% and 96% respectively for the different types of heart disease. This framework enhances the accuracy of the models that are adapted for diagnosing disease with clinical real data [46].

The proposed paper uses retina fundus image to examine the major complications of CVD. Hypertension is the main cause for the disease, it happens due less blood flow into the blood vessels. Retinal fundus image with high-resolution and also the assessment of geometric factors of retinal like diameter, branching angles used in diagnosing

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

CVD risks. Systolic Blood Pressure (SBP) is used to classify the potential risk of CVD combined with Framingham risk score.

To determining adverse risk of CVD like Hypertensive Retinopathy caused by hypertension. And also occurrence of atherosclerotic plaque and inflammatory changes in the arteries will cause the Cholesterol-embolization syndrome (CES). These two major factors can be evaluated or identified easily by the micro structural changes in the optic-disc of retinal vasculature. The proposed computer-aided framework is helps in measuring the changes happen in the retinal vessel in fully-automatic fashion.

Methodology

Network Model

The proposed work constructs GAN synthetic images used for developing Deep Learning (DL) model which promises the researchers to fulfil the clinical findings effectively. The proposed synthesis model will be constructed in data-driven fashion for STARE fundus image benchmark.

The major aim of this work is to automate the process in locating Hypertensive Retinopathy and CES majorly on identification of the anatomical regions of retinal fundus. The second component concerns about the findings to determine a diagnosis. The other output measurements of the anatomical structures will be useful for tracking CVD severity and to recommend the proper treatment over time.

The developed synthetic retinal images are evaluated by a modified Inception V3 architecture DL model as shown in figure1 which allows retraining the existing ImageNet in order to use it for solving custom image classification tasks. DL models will be implemented with Tensorflow libraries and Keras API where all the images are resized to appropriate pixel size which is needed by Keras' API for doing the process. Augmenting of image data may also be proposed to increase the variation level within the training dataset. This kind of data augmentation helps to improve the accuracy and cross-entropy of the model further. The proposed model is trained with stochastic gradient descent in a batch size of 32 images. To optimize the learning rate of the model to be 0.001 adam optimizer is chosen for implementing it. The multi classifier model predicts the risk factors and classifies the disease based on its risk level.

U-Net Generator Model

The generator takes a retinal vessel as an input image. The proposed model is not use a input point of the latent space which can be done in a traditional GAN model. In this U-Net generator, dropout layers are being used to receive the source of randomness of an image which are used both during training and when a prediction is to be made. In the U-Net model the input is from the source image and the output image is in target domain.

The proposed U-Net architecture is applied for the generator phase in GAN network. The other conventional model uses the common encoder-decoder model instead of the generator. An iput image is given to both encoder-decoder generator and U-Net model to down sample it over a few layers upto the bottleneck level. Further, the representation next to the bottleneck is then up sampled again over a few layers. The final image with desired size is obtained in the output. The proposed U-Net model is made this task simple by bringing the links to be of same size between network layers. Thus, it avoids the bottleneck in getting the desired output.

During the Image-to-image translation, the proposed U-Net model arranges same-sized feature maps into the last layer. These feature maps are merged with the decoders. This is repeated with all the layers in the encoder and parallel layer of the decoder, which forms a U-shape to the proposed model.

Anatomical regions of retinal fundus

To make accurate disease prediction, identification of the anatomical regions of retinal fundus has to be done on attention basis of DL model. The proposed work uses soft attention, for generating heatmap which depicts the most predictive image pixels in the retinal image. The model will assess some random retinal images from the data repositories mentioned in the work. In the anatomical locations, all the identified patterns highlighted by the saliency maps are considered for each prediction. During the models training phase the blood vessels found to be highlighted is used to predict risk factors such as age, smoking and SBP [47].

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

Early detection and prevention is essentially being carried out by a large number of dataset. The proposed work ensures improvement of the quality of care, outcome of the patient, specific target prescribed in the database such as monitoring of patients movements and stopping therapies. The proposed model is also observed with the influence of clinical interventions.

Objective Function

The generator G is a mapping function between the retinal image f and an artery vessel image g. It is denoted as, G: f->g. Then, the discriminator denotes as D, which maps a pair of {f,g} to binary Classification $\{0,1\}^N$. The mean value lies between 0 and 1.

- g represents machine-generated or human-annotated artery image
- N represents is the number of decisions.

Number of decisions for Image GAN is equal to 1 and it is represented as N =Width*Height with an image of W*H. The kernel function used in the proposed of GAN model is suitable for segmenting the coronary artery vessels. The proposed GAN model gives solution to the problem of optimization and thus there is no randomness implicated in the generator G. In the proposed GAN, the generator stops the discriminator to do further in making suitable decision on finding unclear outputs to the real data. Hence, the ultimate aim of obtaining realistic outputs from the generator has been achieved.

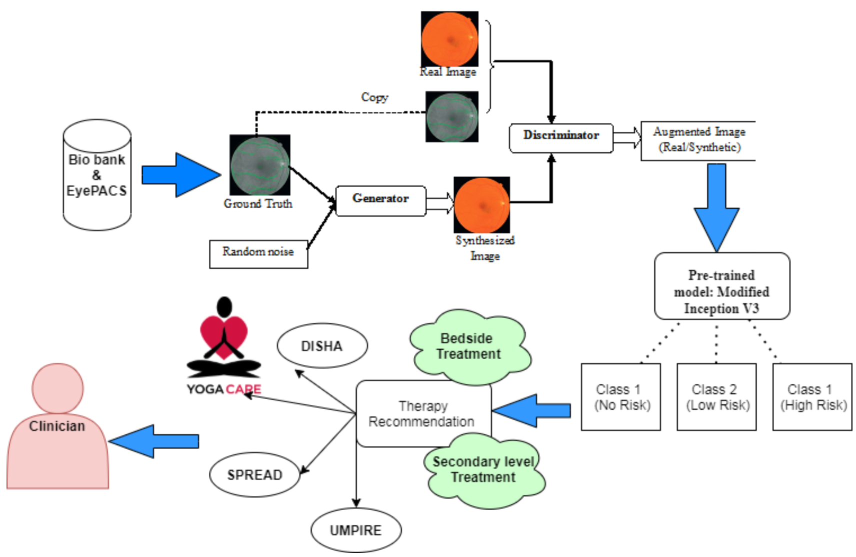

Figure 1 Network Process Flow

The work predicts the CVD with the risk factors from retinal fundus and also will suggestions to the clinicians about the treatment based the prevalence rate of the disease found in the patient is shown in the Figure1. The GAN framework take up input image from online repository UK Biobank and EyePACS a publicly available dataset and do synthesizing high-resolution retinal images which is given to the training phase of the proposed model.

Results

The proposed models performance is compared with different other models which is shown in Table 1 and Table 2. Also the performance measures of various methods in U-Net model and Comparison of precision, recall, dice co-efficient with various network models are shown in Table 1 and Table2 respectively. It is observed that the U-Net model performing lesser with no discriminator, patch GANs is also performing less with both the datasets. Image GAN framework improves quality of image segmentation which also has the most biased capability. The proposed model outperforms other conventional model. The result shows that, the proposed image GAN outperforms

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

and it seems reliable to maintain. It is observed from the experimental result is that a powerful discriminator helps in improving the successful training to the proposed GAN.

Table 1: Performance comparison of U-Net model with different other models

Model	UK Biobank		EyePACS	
	ROC	PR	ROC	PR
U-Net with no discriminator	0.7813	0.7090	0.7589	0.7190
Pixel GAN	0.7876	0.7099	0.7555	0.7077
Patch GAN-1	0.7589	0.7122	0.7665	0.7322
Image GAN	**0.8188**	**0.7997**	**0.8100**	**0.7943**

Table 2: Comparison of various Network models on UK Biobank and EyePACS a publicly available dataset

Model	UK Biobank			EyePACS		
	ROC	PR	Dice	ROC	PR	Dice
AlexNet	0.7706	0.7094	0.7000	-	-	-
CNN	0.7876	0.7099	0.7166	0.7555	0.7077	0.7123
R-CNN	0.7589	0.7122	0.7080	0.7665	0.7322	0.7222
Proposed GAN Network	**0.8088**	**0.7997**	**0.8080**	**0.8100**	**0.7943**	**0.8000**

For further comparison, the proposed work can transformed the probability maps into binary coronary artery images. In this work Otsu threshold has been done. In Fig2 & Fig3 the charts shows that the CNN model usually yields lot of false positives than the proposed method in order to predict the probability maps. In contrast, the proposed method performed well in finding more false negatives rate of artery vessels. The advantage of the proposed work is to assign low probability around uncertain regions of artery vessels since it has appropriate inclination. The Eq.1 is used to calculate the precision performance metric

Precision: It computes the number of positive class predictions that actually belong to the positive class. It can be calculated by usingEq. (1)

$$\text{Precision} = \frac{TP}{TP+FP} \tag{1}$$

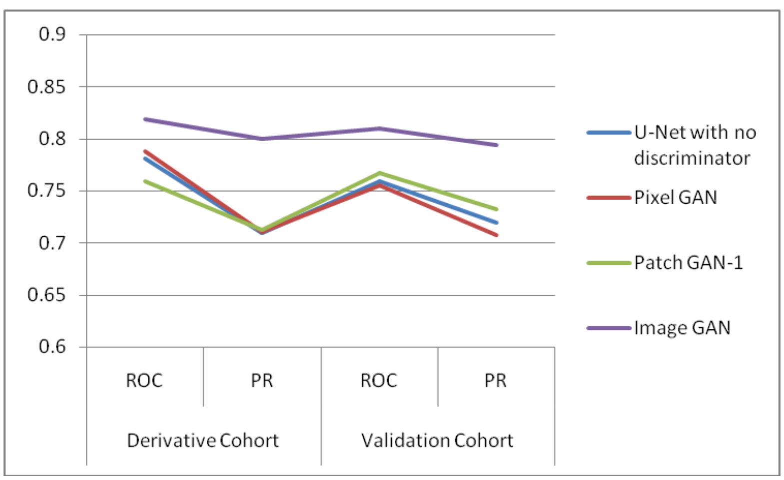

Figure 2: Line Chart between Various Methods of U-Net Model

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 5, 2021, Pages. 2563 - 2572
Received 15 April 2021; Accepted 05 May 2021.

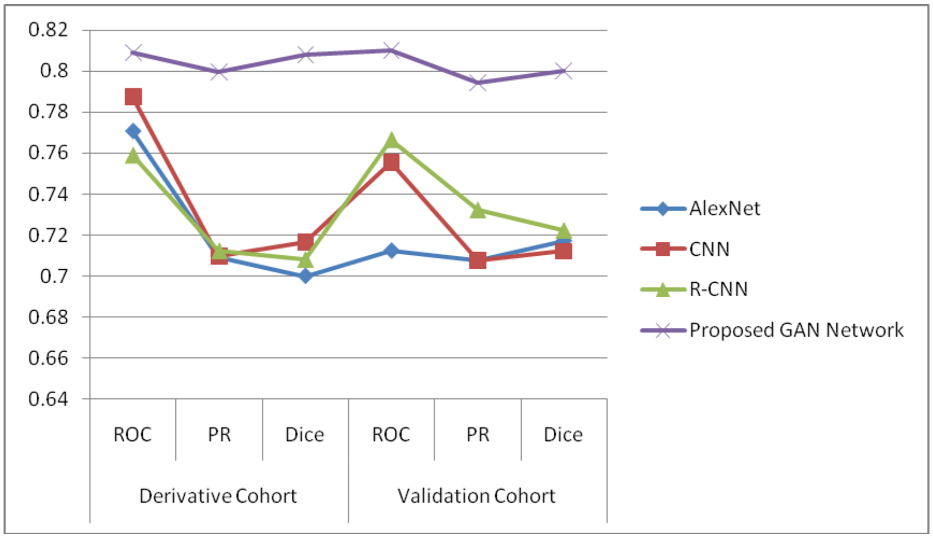

Figure 3: Line Chart between Various Neural Networks with the proposed model

Conclusion

The proposed GANs model is used in segmenting the Retinal fundus vessel with improved experimental results. It suggests that presence of a discriminator in GAN can provide more accuracy in segmenting artery vessels. The proposed U-Net method performed well in predicting the disease when compared with other existing conventional methods. Compared to other existing methods, the proposed method included less false positives at fine arteries. It helps the medical practitioners to predict heart attack much earlier so that patients no need to go for further non invasive tests. In the future work the proposed model expects that additional prior knowledge on the vessel structures on retinal fundus may influence the better performance further.

References

[1] J. Y.-H. Ng, M. Hausknecht, S. Vijayanarasimhan, O. Vinyals, R. Monga, and G. Toderici.(2015). Beyond short snippets: Deep networks for video classification, Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition,IEEE,4694–4702.

[2] Y. Chen, X. Yin, L. Shi, et al. (2013).Improving abdomen tumor low-dose CT images using a fast dictionary learning based processing,Phys. Med. Biol. 58(16), 5803–5820.

[3] M. Liang and X. Hu. (2015). Recurrent convolutional neural network for object recognition, Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, 3367–3375.

[4] W. De Mulder, S. Bethard, and M.-F. Moens. (2015). A survey on the application of recurrent neural networks to statistical language modeling, Computer Speech & Language, 30(1), 61–98.

[5] R. P. Poudel, P. Lamata, and G. Montana. (2016). Recurrent fully convolutional neural networks for multi-slice MRI cardiac segmentation, Reconstruction, Segmentation, and Analysis of Medical Images, Springer, 83–94.

[6] G. Litjens, T. Kooi, B. E. Bejnordi, A. A. A. Setio, F. Ciompi, M. Ghafoorian, J. A. van der Laak, B. van Ginneken, and C. I. Snchez.(2017). A survey on deep learning in medical image analysis, Medical ImageAnalysis, 42(Supplement C), 60 – 88.

[7] Zreik, M., Lessmann, N., van Hamersvelt, R.W., Wolterink, J.M., Voskuil, M., Viergever, M.A., Leiner, T. and Išgum, I.(2018). Deep learning analysis of the myocardium in coronary CT angiography for identification of patients with functionally significant coronary artery stenosis. *Medical image analysis*, *44*, 72-85.

[8] Xie, S., Tu, Z.(2015). Holistically-nested edge detection. Proceedings of the IEEE International Conference on Computer Vision, 1395-1403.

[9] Majd Zreik, Robbert W. van Hamersvelt, Jelmer M. Wolterink, Tim Leiner, Max A. Viergever, Ivana Išgum.(2019). A Recurrent CNN for Automatic Detection and Classification of Coronary Artery Plaque and Stenosis in Coronary CT Angiography, Published in IEEE Transactions on Medical Imaging.

[10] Richardson, W.S., Glasziou, P., Polashenski, W.A. and Wilson, M.C. (2000). A new arrival: evidence about differential diagnosis. *BMJ Evidence-Based Medicine*, *5*(6),164-165.

[11] Evangelos K Oikonomou*, Mohamed Marwan*, Milind Y Desai*, Jennifer Mancio, Alaa Alashi, Erika Hutt Centeno, Sheena Thomas, Laura Herdman, Christos P Kotanidis, Katharine E Thomas, Brian P Griffin, Scott D Flamm, Alexios S Antonopoulos, Cheerag Shirodaria, Nikant Sabharwal, John Deanfield, Stefan Neubauer, Jemma C Hopewell, Keith M Channon, Stephan Achenbach, Charalambos Antoniades, (2018). Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data, Published online, http://dx.doi.org/10.1016/S0140-6736(18)31114-0

[12] J. Ma, J. Huang, Q. Feng, et al.(2011). Low-dose computed tomography image restoration using previous normal-dose scan, Med. Phys. 38(10), 5713-5731.

[13] G. Raff, A. Abidov, S. Achenbach, D. Berman, L. Boxt, M. Budoff, V. Cheng, T. DeFrance, J. Hellinger, R. Karlsberg et al.(2009). SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography, Journal of Cardiovascular Computed Tomography, 3(2), 122–136.

[14] S. Achenbach.(2018), Can CT detect the vulnerable coronary plaque?,The International Journal of Cardiovascular Imaging (formerly Cardiac Imaging), 24(3), 311–312.

[15] Gilbert L. Raff, MD*, Chair, Aiden Abidov, MD, PhD, Stephan Achenbach, MD, Daniel S. Berman, MD, Lawrence M. Boxt, MD, Matthew J. Budoff, MD, Victor Cheng, MD, Tony DeFrance, MD, Jeffrey C. Hellinger, MD, Ronald P. Karlsberg, MD. SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography, Society of Cardiovascular Computed Tomography, 2400 N Street NW, Washington, DC 20037, USA.

[16] Van Hamersvelt, R.W., Zreik, M., Voskuil, M., Viergever, M.A., Išgum, I. and Leiner, T.(2018). Deep learning analysis of left ventricular myocardium in CT angiographic intermediate-degree coronary stenosis improves the diagnostic accuracy for identification of functionally significant stenosis. *European radiology*,1-10.

[17] Nguyen, U.T., Bhuiyan, A., Park, L.A., Ramamohanarao, K.(2013). An effective retinal blood vessel segmentation method using multi-scale line detection. Pattern recognition, 46(3), 703-715.

[18] Fu, H., Xu, Y., Lin, S., Wong, D.W.K., Liu, J., (2016). Deepvessel Retinal vessel segmentation via deep learning and conditional random field, International Conference on Medical Image Computing and Computer-Assisted Intervention, 132-139.

[19] Wu, D., Wang, X., Bai, J., Xu, X., Ouyang, B., Li, Y., Zhang, H., Song, Q., Cao, K. and Yin, Y.(2019). Automated anatomical labeling of coronary arteries via bidirectional tree LSTMs, *International journal of computer assisted radiology and surgery*, *14*(2), 271-280.

[20] A. Cassar, D. R. Holmes Jr, C. S. Rihal, and B. J. Gersh. (2009). Chronic coronary artery disease: diagnosis and management, Mayo Clinic Proceedings, 84(12), 1130–1146.

[21] P. F. Feruglio, C. Vinegoni, J. Gros, et al.(2010). Block matching 3D random noise filtering for absorption optical projection tomography, Phys. Med. Biol. 55(18), 5401-5415.

[22] D. Kang, P. Slomka, R. Nakazato, et al.(2013). Image denoising of low-radiation dose coronary CT angiography by an adaptive block-matching 3D algorithm,Proc. SPIE 8669, Medical Imaging 2013:Image Processing, 86692G.

[23] Tian, C., Xu, Y., Fei, L. and Yan, K.(2018). Deep Learning for Image Denoising: A Survey. *arXiv preprint arXiv:1810.05052*.

[24] Maninis, K.K., Pont-Tuset, J., Arbel_aez, P., Van Gool, L.(2016).Deep retinal image understanding. In: International Conference on Medical Image Computing and Computer-Assisted Intervention,140-148.

[25] Melin_s_cak, M., Prenta_si_c, P., Lon_cari_c, S.(2015), Retinal vessel segmentation using deep neural networks. In: VISAPP 2015 (10th International Conference on Computer Vision Theory and Applications).
[26] S. Andermatt, S. Pezold, and P. Cattin.(2016), Multi-dimensional gated recurrent units for the segmentation of biomedical 3D-data, Deep Learning and Data Labeling for Medical Applications. Springer,142–151.
[27] W. Xue, G. Brahm, S. Pandey, S. Leung, and S. Li, "Full left ventricle quantification via deep multitask relationships learning," Medical Image Analysis, vol. 43, pp. 54–65, 2018.
[28] Chen, H., Zhang, Y., Zhang, W., Liao, P., Li, K., Zhou, J. and Wang, G., (2017). Low-dose CT via convolutional neural network. Biomedical optics express, 8(2), 679-694.
[29] Z. Li, L. Yu, J. D. Trzasko, et al.(2014). Adaptive nonlocal means filtering based on local noise level for CT denoising, Med. Phys. 41(1), 011908.
[30] M. Aharon, M. Elad, and A. Bruckstein. (2016).K-SVD: An algorithm for designing overcomplete dictionaries for sparse representation, IEEE Trans. Signal Process. 54(11), 4311-322.
[31] A. Karpathy and L. Fei-Fei. (2015). Deep visual-semantic alignments for generating image descriptions, Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, 3128–3137.
[32] Ricci, E., Perfetti, R. (2007). Retinal blood vessel segmentation using line operators and support vector classification. IEEE transactions on medical imaging, 26(10), 1357-1365.
[33] Soares, J.V., Leandro, J.J., Cesar, R.M., Jelinek, H.F., Cree, M.J.(2006). Retinal vessel segmentation using the 2-d gabor wavelet and supervised classification. IEEE Transactions on medical Imaging, 25(9), 1214-1222.
[34] Zhang, B., Zhang, L., Zhang, L., Karray, F.(2010). Retinal vessel extraction by matched filter with first-order derivative of gaussian. Computers in biology and medicine, 40(4), 438-445.
[35] Becker, C., Rigamonti, R., Lepetit, V., Fua, P.,(2013). Supervised feature learning for curvilinear structure segmentation. In: International Conference on Medical Image Computing and Computer-Assisted Intervention, 526-533. Springer.
[36] Ronneberger, O., Fischer, P., Brox, T.:(2015). U-net: Convolutional networks for biomedical image segmentation. In: International Conference on Medical Image Computing and Computer-Assisted Intervention, Springer, 234-241.
[37] He, K., Zhang, X., Ren, S., Sun, J.(2016). Deep residual learning for image recognition, Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, 770-778.
[38] Fu, H., Xu, Y., Lin, S., Wong, D.W.K., Liu, J.(2016). Deepvessel: Retinal vessel segmentation via deep learning and conditional random field. In: International Conferenceon Medical Image Computing and Computer-Assisted Intervention, Springer, 132-139.
[39] Xie, S., Tu, Z.: Holistically-nested edge detection. In: Proceedings of the IEEE, International Conference on Computer Vision. pp. 1395-1403 (2015).
[40] Goodfellow, I., Pouget-Abadie, J., Mirza, M., Xu, B., Warde-Farley, D., Ozair, S., Courville, A., Bengio, Y.(2014). Generative adversarial nets. In: Advances in neural information processing systems, 2672-2680.
[41] Y. Chen, Z. Yang, Y, Hu et al. (2012). Thoracic low-dose CT image processing using an artifact suppressed large-scale nonlocal means, Phys. Med. Biol. 57(9), 2667-2688.
[42] Deepa, T., Sathiyabhama, B., Akilandeswari, J. and Gopalan, N.P., (2014). Action fuzzy rule based classifier for analysis of dermatology databases, *International Journal of Biomedical Engineering and Technology*, *15*(4), 360-379.
[43] Ryan Poplin, Avinash V. Varadarajan,Katy Blumer1, Yun Liu1, Michael V. McConnell, Greg S. Corrado, Lily Peng, and Dale R. Webster.(2018). Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning, Nature Biomedical Engineering, https://doi.org/10.1038/s41551-018-0195-0.
[44] Daniel S.W. Ting, Lily Peng, Avinash V. Varadarajan, Tin Yan Alvin Liu.(2019). Novel Retinal Imaging in Assessment of Cardiovascular Risk Factors and Systemic Vascular Diseases, Diabetic Retinopathy and Cardiovascular Disease. Front Diabetes. Basel, Karger, 27, 106–118, DOI: 10.1159/000486269.
[45] Krishnan, M N. (2012). Coronary heart disease and risk factors in India - on the brink of an epidemic?. Indian heart journal, 64(4), 364-7. doi:10.1016/j.ihj.2012.07.001.

[46] Baccouche, A., Garcia-Zapirain, B., Castillo Olea, C. and Elmaghraby, A. (2020). Ensemble Deep Learning Models for Heart Disease Classification: A Case Study from Mexico. Information, 11(4), 207.

[47] Simonyan K, Vedaldi A, Zisserman A.(2017). Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps. Computer Vision and Pattern Recognition (csCV).

[48] B. Sathiyabhama, J. Jayanthi, T. Sathiya, A. K. Ilavarasi, S. Udhaya Kumar, V. Yuvarajan, Konga Gopikrishna, "A novel Feature Selection Framework based on Grey Wolf Optimizer for Mammogram Image Analysis", Journal of Neural Computing and Applications, 2020

[49] B. Sathiyabhama, J. Jayanthi, T. Sathiya, A. K. Ilavarasi, S. Udhaya Kumar, V. Yuvarajan, "A grey wolf optimization for feature subset selection in the classification of breast cancer data" , Journal of Soft Computing, 2020

[50] Sennan, S., Ramasubbareddy, S., Balasubramaniyam, S., Nayyar, A., Abouhawwash, M., & Hikal, N. A. (2021). T2FL-PSO: Type-2 Fuzzy Logic-based Particle Swarm Optimization Algorithm used to Maximize the Lifetime of Internet of Things. IEEE Access, 9(1), 63966-63979.

[51] Sankar, S., Srinivasan, P., Luhach, A. K., Somula, R., & Chilamkurti, N. (2020). Energy-aware grid-based data aggregation scheme in routing protocol for agricultural internet of things. Sustainable Computing: Informatics and Systems, 28, 100422.

[52] Sennan, S., Somula, R., Luhach, A. K., Deverajan, G. G., Alnumay, W., Jhanjhi, N. Z., & Sharma, P. (2020). Energy efficient optimal parent selection based routing protocol for Internet of Things using firefly optimization algorithm. Transactions on Emerging Telecommunications Technologies, e4171.

[53] Asraf Yasmin, B., Latha, R., & Manikandan, R. (2019). Implementation of Affective Knowledge for any Geo Location Based on Emotional Intelligence using GPS. International Journal of Innovative Technology and Exploring Engineering, 8(11S), 764–769. https://doi.org/10.35940/ijitee.k1134.09811s19

[54] Muruganantham Ponnusamy, Dr. A. Senthilkumar, & Dr.R.Manikandan. (2021). Detection of Selfish Nodes Through Reputation Model In Mobile Adhoc Network - MANET. Turkish Journal of Computer and Mathematics Education, 12(9), 2404–2410. https://turcomat.org/index.php/turkbilmat/article/view/3720