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Diagnosis of Coronary Artery Disease from Myocardial Perfusion Imaging Using Convolutional Neural Networks

Vincent Peter C. Magboo[a,] *, Ma. Sheila A. Magboo[a]

[a] *Department of Physical Sciences and Mathematics, University of the Philippines Manila Padre Faura St., Ermita, Manila, 1000, Philippines*

Abstract

Cardiovascular disease is a highly prevalent health problem in both underdeveloped and developing countries worldwide. As such, it remains to be one of the top health priorities in many countries. In coronary artery disease (CAD), the formation of an atherosclerotic plaque is evident in the lumen of blood vessels leading to the derangement in blood flow resulting to diminished delivery of oxygen to the myocardium. Single Photon Emission Computed Tomography – Myocardial Perfusion Imaging (SPECT-MPI) is a usually requested imaging modality to evaluate for CAD. Visual evaluation of the MPI images is performed by a nuclear medicine doctor and is largely dependent on his experience showing significant inter-observer variability. The study aims to assess the performance of convolutional neural networks (CNN) using transfer learning to classify SPECT-MPI for perfusion abnormalities using an anonymized publicly available SPECT-MPI dataset. The pre-processing methods that were applied to the dataset were the following: (a) normalization of images, (b) shuffling of images, (c) train-test split, and (d) geometric augmentation. The pre-processed data was then entered to the popular pre-trained CNNs typically applied to medical images: VGG16, DenseNet121, InceptionV3 and ResNet50. The best performing models were obtained by VGG16 and InceptionV3 with the highest accuracy rate of 84.38%. However, VGG16 had higher recall and F1-scores as compared to InceptionV3 while InceptionV3 had higher precision. Nonetheless, VGG16, InceptionV3 and DenseNet121 obtained similar performance metrics with each other (recall:80-100%, precision: 80.65-100%, F1-scores: 88.89-90.91%) while ResNet50 generated the lowest performance metrics. Overall findings suggest that any of these 3 CNN models (VGG16, InceptionV3, DenseNet121) can be deployed by nuclear medicine physicians in their clinical practice to further augment their decision skills in the interpretation of SPECT-MPI tests. The models can also be adopted as dependable and trusted secondary assessment which can guide junior doctors seeking consultation for a reliable diagnosis. These models can likewise serve as teaching or learning materials for the less experienced physicians particularly those still in their training career. This highlights the clinical utility of these models in the practice of nuclear cardiology. The results of the research exhibited encouraging outcomes which may possibly be incorporated clinical work. The study has the potential to enrich CAD discernment and monitoring.

* Corresponding author. Tel.: +0-000-000-0000 ; fax: +0-000-000-0000 .
E-mail address: vcmagboo@up.edu.ph

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1. Introduction

Coronary Artery Disease (CAD) is a highly prevalent health problem being one of the top causes of death and

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sickness in both developed and developing countries worldwide [1]. As such, it remains to be one to the top health priorities in many countries. In CAD, there is a formation of atherosclerotic plaque in the lumen of blood vessels leading to the derangement in blood flow resulting to diminished delivery of oxygen to the myocardium [2]. The obstruction in the coronary vessels results to myocardial ischemia where there is impairment of the functions of the heart. In its severe form, the ischemia can further lead to unwanted cardiac events such as myocardial infarction, lengthy hospitalization, chronic heart failure, and sudden cardiac death [1, 3]. Non-invasive imaging modalities are usually requested by cardiologists not only to make a diagnosis of CAD but also for prognosis indicator, selection for patients for revascularization procedures and appraising acute coronary syndromes [4]. A typically requested laboratory test to evaluate CAD is the Single Photon Emission Computed Tomography – Myocardial Perfusion Imaging (SPECT-MPI). This imaging test details on the spread of the tracer in the myocardium and a cost- effective modality for evaluating the extent of CAD prior to a highly invasive coronary angiography, thus reducing number of unnecessary angiographies as well as enabling appropriate treatments [5]. The myocardial perfusion is assessed by examining the distribution of the radiotracer in the myocardium. To determine the areas with diminished perfusion, the myocardium is imaged at rest as well as at stress. The assessment of the SPECT-MPI images in various dimensions (horizontal long axis (HLA), vertical long axis (HLA) and short axis (SA)) is performed visually by a nuclear medicine physician. This evaluation is largely contingent on the physician's experience and showing substantial inter-observer variability [6]. It is in this area of classification of SPECT-MPI images where deep learning (DL) can be utilized, thus enabling patients to responsibly keep track their lifestyle habits, mitigate the potential adverse complications of CAD as well as enhancing the whole diagnostic process leading to institution of the much-needed early medical therapy to increase survivorship and/or ameliorate overall well-being of patients with CAD [7 - 8]. To guide doctors in the evaluation of CAD, the use of convolutional neural networks (CNN) can be harnessed resulting to an improved reliability of MPI. Understanding the underlying factors regarding myocardial perfusion abnormalities remains to be a crucial challenge not only among health professionals but to data science enthusiasts as well since many research tasks in medicine now encompass the use of several combinations of machine learning, deep learning, and statistical methods in the hope of improving disease detection [9 - 12].

The goal of this research is to explore the diagnostic capability of CNN via transfer learning in the classification of SPECT-MPI for perfusion abnormalities. Performance metrics consist of accuracy, recall, F1-score, and precision. The notable contribution of this research work is the formation of simple, valid, and reliable CNN models for the evaluation of CAD with acceptable performance metrics which can be used as decision-support tool in clinical practice by physicians.

This research study is presented in this manner: Section 2 presents the latest relevant works in the application of deep learning in nuclear cardiology. Section 3 focuses on the methodology used in this research on SPECT- MPI classification. This includes the different pre-processing steps done on the dataset and the CNN architectures used in the classification for CAD. Section 4 highlights all outcomes of the various simulation experiments and the exhaustive discussion regarding the analysis. The conclusions of the research are discussed in Section 5, which also specify the subsequent research work.

2. Related Literature

Artificial intelligence techniques have been achieving increased distinction in medicine as data becomes progressively sophisticated. These methods can attenuate the importance of cardiovascular imaging by computerizing many steps, looking for new patterns in data as well as suggesting alternative assessment [13]. Papandrianos and Papageorgiou [4] applied a deep learning approach to classify SPECT-MPI images as normal or abnormal with a 93.47$\pm$ 2.81 accuracy rate and an area under the receiver operating characteristic curve (AUC) of 0.936. Authors concluded that their CNN model is an efficient deep neural network capable of examining perfusion problems related to myocardial perfusion problems on SPECT images. In [5], authors utilized pre-trained deep neural networks to identify perfusion abnormalities with 94% accuracy, 88% sensitivity and 100% specificity. Authors reported that their proposed models could assist in judgement call for the evaluation of SPECT-MPI for myocardial perfusion problems. In the study by Teuho et al., CNN was also used in the classification of polar maps for myocardial ischemia [14]. The study obtained 82.61% accuracy, 0.8058 AUC, 76.47% F1-score, 65% sensitivity, 96.15% specificity and 93.75% precision. This suggests that classification of ischemia is feasible using polar maps alone with a custom CNN.

In the study of Mostafapour et al., the effect of attenuation correction (AC) in SPECT-MPI images was analyzed using ResNet and UNet deep CNN [15]. Authors concluded that deep learning AC approaches could determine reliable AC in MPI-SPECT imaging. In [16], a simple CNN for the assessment of SPECT-MPI images into binary categories (normal, ischemia) was studied. After application of data augmentation technique (rotating and zooming randomly), an exploratory approach assessing various number of layers, dense nodes, batch size and pixel size were done. The results of the study obtained 90.20% accuracy and a 0.9377 AUC. Authors further considered their CNN model to be a very useful adjunctive solution for this classification challenge, as it can generate valid and dependable performance compared to traditional clinical approaches. Chen et al., applied CNN in the assessment of myocardial perfusion images for CAD which generated 87.64% accuracy, 81.58% sensitivity, and 92.16% specificity. Authors reported their model to significantly diminished the time required for physician to come up with an image assessment, write official reports and thus, can help physicians in evaluating coronary heart diseases accurately in clinical practice [17].

Another study applying ML models to SPECT-MPI polar maps for coronary artery disease was made by de Souza Filho et al. [18]. Four ML models were tested in this study which showed random forest with the best performance of 93.8% accuracy, 96.3% sensitivity, 96.8% precision and 0.853 AUC. Kikuchi et al. applied U-Net and U-Net++ architectures for cardiac perfusion segmentation from SPECT-MPI images to diminish the consequent problems of extra-cardiac activity [19]. The results showed a Dice coefficient of 0.918 with a highly reliable myocardial region extraction thereby significantly shrinking the extracardiac activity which interferes in the evaluation of SPECT-MPI images. In [20], authors applied CNN in the diagnosis of CAD from SPECT-MPI images which obtained a 0.872 AUC, 82.7% accuracy, 74.4% sensitivity and 84.9% specificity. In [21], authors suggested a deep learning approach using an Oura smart ring to quickly assess COVID-19. With the assistance of recurrent neural network and CNN models, a rapid test is prepared in the laboratory which has decreased the error rates for quick and reliable diagnosis. Shabaz et al. [22], reported that by exploiting the interdisciplinary fields of machine learning, neuroscience, healthcare, and engineering, authors created engaging programs which may hasten neuroscience rollout using advances in multimedia for health care.

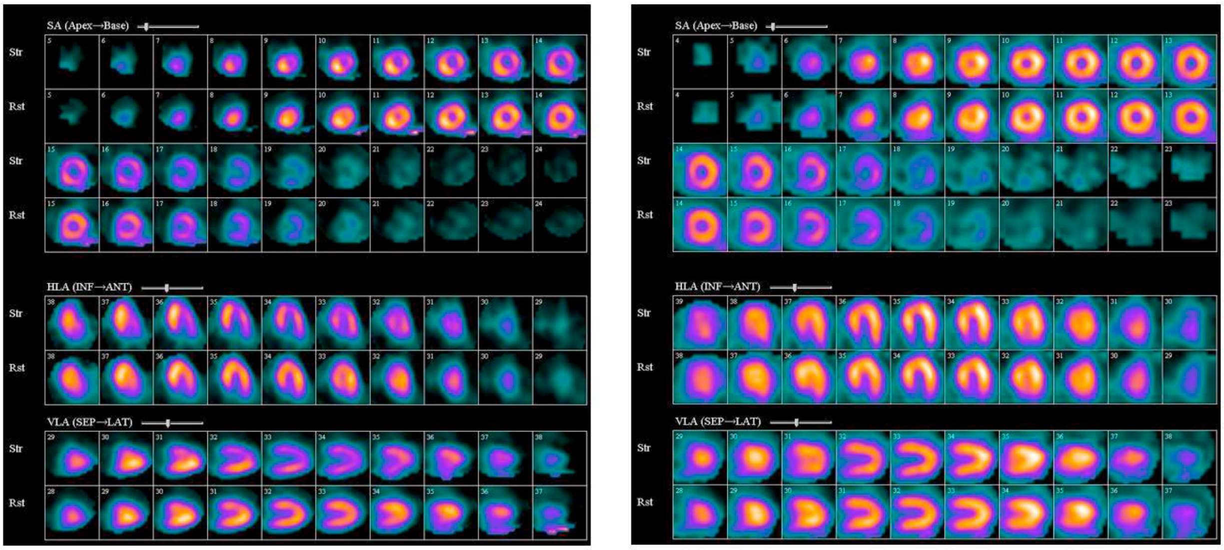
3. Methodology

The machine learning framework for this study is shown in Fig 1. After downloading the SPECT-MPI data images from a machine learning repository, various pre-processing steps (normalization, data shuffling, and geometric augmentation techniques) were applied to the images. Following a train-test split, the pre-processed data was then entered to the popular pre-trained CNNs used in medical imaging: VGG16, DenseNet121, InceptionV3 and ResNet50. Assessment of diagnostic performance of the CNN models was then obtained.

Fig. 1. Machine Learning Pipeline for CAD Diagnosis

3.1. Dataset Description

In this study, an anonymized publicly available SPECT-MPI dataset from a machine learning data repository (https://www.kaggle.com/selcankaplan/spect-mpi) was used [23]. The dataset contained 192 patients who underwent stress-test-rest Tc99m MPI. There was also imbalance with 150 patients (78%) having coronary artery disease while 42 patients (22%) do not have coronary artery disease). Fig 2 shows a sample SPECT-MPI image with and without CAD. The assessment of the images for perfusion defects is made by nuclear medicine physicians where the SPECT-MPI images are visually compared between stress and rest across all dimensions (HLA, VLA, SA). An abnormality in perfusion identified in stress but not in rest images is classified as ischemia while an abnormality identified in both stress and rest images is called an infarction. For this study, SPECT-MPI images with ischemia and/or infarction is diagnosed as having CAD while those images without perfusion defects are classified as not having CAD.



With CAD Without CAD

Fig. 2 Sample SPECT-MPI Images with and without CAD

3.2. Preprocessing Steps

The preprocessing steps applied to the images were the following: (a) normalization of images, (b) shuffling of images (c) splitting of dataset into training and testing, and (d) geometric augmentation. The Min-Max normalization was utilized for normalizing the images. To generate a casual order of images, the ImageDataGenerator's shuffling technique from keras.preprocessing.image library was employed. The dataset was divided into three sections: testing (20%) and the remainder (80%) was further divided into 80% training and 20% validation. The typical geometric augmentations such as: (1) shear range = +0.30, (2) horizontal flipping, (3) rotation range = +15, (4) zoom range = +0.15, and (5) translation = +0.15 were applied to the images in the training set using also the ImageDataGenerator.

3.3. Pre-Trained Models

In this research work, four pre-trained architectures namely: DenseNet121, ResNet50, InceptionV3, and VGG16 were applied to the SPECT-MPI dataset. Based on the initial exploratory simulations, the following were defined as the optimum values for the parameters of the various pre-trained models: input pixel size at 256 x 256 x 3, number of epochs at 50, learning rate at 0.001, batch size at 32, dense nodes at 256, 128 and 64 and drop out at 0.3. The activation function was ReLu whereas in the output layer, sigmoid was adopted. The loss function utilized was the binary cross-entropy and the optimizer employed was Adam.

ResNet50, is a 50-weight layer network having 2.3 x 10^7 trainable parameters [24 - 25]. The ResNet architecture has been instituted to answer the vanishing degradation issue of model training that causes performance deterioration in the models [26]. ResNet models make use of identity shortcut connections that jump over one or more layers providing detour for gradients to pass through without diminishing [27]. VGG16 is an extension of Visual Geometry Group consists of 16 weight layers and usually constructed using 3 x 3 convolutional layers piled on each other [24 - 25]. In the midst of these layers, ReLu is adopted as the activation function and then followed by three fully-connected layers holding many of the network parameters [28]. VGG16 architecture contains 1.3 x 10^8 trainable free parameters [24 - 25]. VGG16 is usually applied in image recognition problems as it has a network composition that is easier to reconfigure [28]. VGG16 has also been reported to suitable for medical image classification due to its balance of accuracy and efficiency preferring them particularly for mobile networked applications [29]. DenseNet 121 comprises of 121 layers having more than 8 million parameters. DenseNet121 is partitioned into DenseBlocks with feature maps having same dimensions in the block but with different number of filters. The transition layers in between blocks apply batch normalization for down-sampling [30]. DenseNet has been used in studies involving medical imaging as it weakens the issue of vanishing gradient, enhances feature reuse, decrease parameter handling, all beneficial for training deep learning models. Likewise, it links each layer to all layers instead of only one final layer enabling it capture image information more in comparison with traditional image processing methods [31]. InceptionV3 is a 48-layer deep network originating from GoogleNet Architecture and has fewer parameters (2.1 x 10^7 trainable free parameters) [25]. Each module totaling 11 modules is composed of convolutional filters, pooling layers and ReLu activation function [28]. Introduced in 2015, it uses modules with only a few weights making it worthy for mobile applications [29].

3.4. Performance Metrics

The CNN models for diagnosis of CAD were evaluated using accuracy, precision, F1-scores and recall. The confusion matrix was also obtained.

3.5. Technical Requirements

All simulation experiments were executed in Kaggle for the free use of GPUs. Python language 3.7.10, TensorFlow 2.6.0, and Keras 2.6.0, were utilized in the simulation experiments.

4. Results and Discussion

There were 192 patient images included in the neural network model building. Four pre-trained CNN architectures were tested (VGG16, InceptionV3, DenseNet121 and ResNet50). The comparative performance metrics are shown in Fig 3. The best performing models were obtained by VGG16 and InceptionV3 with the highest accuracy rate of 84.38%. However, VGG16 had higher recall (100% vs 80%) and F1-scores (90.91% vs 88.89%) as compared to InceptionV3. On the other hand, InceptionV3 has higher precision than VGG16. Nonetheless, VGG16, InceptionV3, and DenseNet121 generated similar performance metrics with each other while ResNet50 had the lowest performance metrics. The confusion matrix of the top three CNN models is presented in Table 1. The results of the simulation experiments were comparable to results generated by the study in [5, 20] but lower when compared with the study in [4] when it comes to VGG16 and InceptionV3. These works made use of transfer learning in CNN for CAD diagnosis [4 - 5, 20]. While there had been many published works in CAD diagnosis, there are only very few studies that apply CNN using purely SPECT-MPI images.

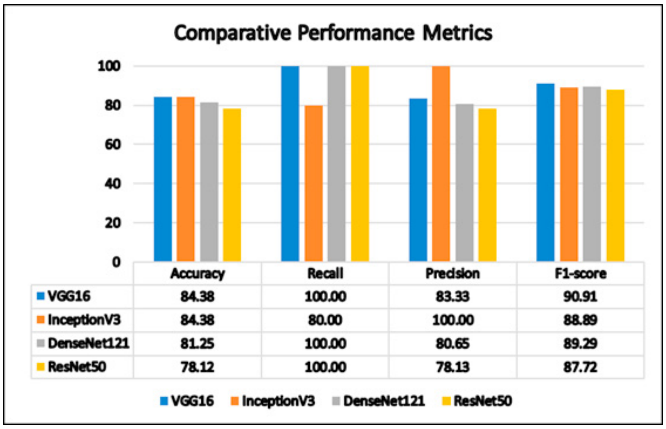


Fig. 3. Comparative Performance Metrics of Various Pre-Trained Architectures for CAD Diagnosis

Table 1. Confusion Matrix of the best CNN Models

	InceptionV3		VGG16		DenseNet121	
	Predicted +	Predicted -	Predicted +	Predicted -	Predicted +	Predicted -
Actual +	[[20	5]	[[25	0]	[[25	0]
Actual -	[0	7]]	[5	2]]	[6	1]]

The comparable performance metrics of these 3 CNN models (VGG16, InceptionV3, DenseNet121) indicate that any of these models can be utilized by nuclear medicine physicians in their clinical practice to further augment their decision skills in the interpretation of SPECT-MPI tests. The simulation experimental results suggest that these models can be valid and dependable tools for the automatic evaluation of SPECT-MPI images. These models can likewise serve as teaching or learning materials for less experienced physicians particularly those in their training career. The models can also be adopted as dependable and trusted secondary assessments which can guide junior doctors seeking consultation for a reliable diagnosis [7]. These highlights the clinical utility of these models in the practice of nuclear cardiology.

SPECT-MPI is a non-invasive modality that provides essential information in CAD enabling physicians to identify perfusion defects thus, having an important role in risk stratification for CAD [13]. The use of CNN has shown its capability to generate adequate and much improved diagnostic performance and consistency for myocardial perfusion defects thus demonstrating its usefulness in nuclear medicine imaging for the assessment of CAD [16, 20]. The use of transfer learning via pre-trained architectures in the classification of SPECT-MPI images for CAD allows researchers to avoid training a base model network with randomly initialized weights [4]. These pre-trained models were trained by the ImageNet dataset. The terminal fully connected layer and the final output (classification) layer are substituted with newer additional layers reshaped to the SPECT-MPI data in transfer learning, that is to master the patterns specific to the SPECT-MPI dataset [5]. Kim et al. suggested ways to choose base CNN models, to adjust them appropriately with careful deliberation of attributes and upgrading solely the terminal fully connected layers of the selected model. Authors further claimed that in cases where model performance must be improved, the model should be adjusted by piecemeal unblocking of the convolutional layers altogether with a decreased learning rate, thus, saving algorithmic costs without diminishing the predictive capabilities [32]. As a result of transfer learning, classification is faster even with a small number of images typically seen in publicly available medical image datasets.

The pre-trained architectures used in this study are typically employed in the classification of medical images ranging from histopathological to radiological images which demonstrate their usefulness as adjunct tools for interpreting physicians [4 – 7, 10, 14 -20, 24- 36]. It is also worth noting that these pre-trained models do not rely on polar maps, gender and gamma camera machine configurations used in SPECT-MPI possibly amplifying the number of parameters [4 - 5]. CNN models with acceptable performance and stability can be generated using deep learning techniques notwithstanding fewer images in the dataset, which more often outperform traditional machine learning models [16, 37]. Otaki et al. claimed that the use of deep learning approaches can remarkably surpass the performance of employing quantitative analysis and the visual comparison for SPECT-MPI [38]. In the study of Apostolopoulos et al., authors have reported that it is possible to classify a small dataset of SPECT-MPI images at a level competing with experts' diagnostic ability using deep learning methods, employing transfer learning and data augmentation techniques [39]. Authors have indicated the use of CNN models to support clinical diagnosis of CAD as support tools and to serve as teaching material.

5. Conclusions and Recommendations

Various CNN models were applied in the SPECT-MPI dataset to make a diagnosis of presence of CAD in these patients. The best performing models were given by VGG16 and InceptionV3 having obtained the highest accuracy of 84.38%. Nonetheless, VGG16, InceptionV3 and DenseNet121 generated comparable performance metrics (recall: 80-100%, precision: 80.65-100%, F1-scores: 88.89-90.91%). Hence, any of these CNN models can be deployed by physicians in their clinical practice to further augment their decision skills in the interpretation of SPECT-MPI tests. The results of this study showed encouraging insights particularly when incorporated in clinical work. The study is likely to enrich CAD recognition and surveillance. For future subsequent work, plans to further ameliorate the diagnostic capability of the proposed models by utilizing larger datasets and considering combining clinical data with perfusion data are being contemplated. It is also recommended to evaluate a dataset of SPECT images which utilize coronary angiography as the more objective gold standard rather than an expert reader evaluation. Likewise, the use of explainable AI tools to be incorporated in the models is also suggested to for better understanding of physicians in the interpretation of the logic behind the classification of these CNN models which would lead to the utilization and incorporation of deep learning tools in clinical practice.

References

[1] Ties, D., van Dorp, P., Pundziute, G., et al. (2022) "Early detection of obstructive coronary artery disease in the asymptomatic high-risk population: objectives and study design of the EARLY-SYNERGY trial." *American Heart Journal* **246 (2022)** : 166-177. https://doi.org/10.1016/j.ahj.2022.01.005

[2] Shahjehan RD, and Beenish S. Bhutta. Coronary Artery Disease. [Updated 2022 Feb 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564304/

[3] Moran A. E., Forouzanfar M. H., Roth G. A., Mensah, G.A., Ezzati, M., Murray, C.J.L., and Mohsen Naghavi. (2014). "Temporal Trends in Ischemic Heart Disease Mortality in 21 World Regions, 1980 to 2010." *Circulation* **129 (14) :** 1483–1492. https://doi.org/10.1161/CIRCULATIONAHA.113.004042

[4] Papandrianos, N., and Elpiniki Papageorgiou. (2021). "Automatic Diagnosis of Coronary Artery Disease in SPECT Myocardial Perfusion Imaging Employing Deep Learning." *Applied Sciences*. **11 (14)** : 6362. https://doi.org/10.3390/app11146362

[5] Berkaya, S.K., Sivrikoz, I.A., and Serkan Gunal. (2020). "Classification models for SPECT myocardial perfusion imaging." *Computers in Biology and Medicine* **123** : 103893. https://doi.org/10.1016/j.compbiomed.2020.103893

[6] Spier, N., Nekolla, S., Rupprecht, C., Mustafa, M., Navab, N., and Maximilian Baub. (2019) "Classification of Polar Maps from Cardiac Perfusion Imaging with Graph-Convolutional Neural Networks." *Scientific Reports* **9 :** 7569. https://doi.org/10.1038/s41598-019-43951-8

[7] Magboo, V.P.C., and Patricia Angela R. Abu. (2022). "Deep Neural Network for Diagnosis of Bone Metastasis." *In 2022 The 5th International Conference on Software Engineering and Information Management (ICSIM) (ICSIM 2022). Association for Computing Machinery, New York, NY, USA*, 144-151. https://doi.org/10.1145/3520084.3520107

[8] Magboo, V.P.C., and Ma. Sheila A. Magboo. (2021). "Imputation Techniques and Recursive Feature Elimination in Machine Learning Applied to Type II Diabetes Classification." *In 2021 4th Artificial Intelligence and Cloud Computing Conference (AICCC '21). Association for Computing Machinery, New York, NY, USA*, 201–207. https://doi.org/10.1145/3508259.3508288

[9] Magboo M.S.A., and Andrei D. Coronel. (2019) "Data Mining Electronic Health Records to Support Evidence-Based Clinical Decisions." *In: Chen YW., Zimmermann A., Howlett R., Jain L. (eds) Innovation in Medicine and Healthcare Systems, and Multimedia. Smart Innovation, Systems and Technologies*, **145**. Springer, Singapore. https://doi.org/10.1007/978-981-13-8566-7_22

[10] Lopez, K.M.M., and Ma. Sheila A. Magboo. (2020). "A Clinical Decision Support Tool to Detect Invasive Ductal Carcinoma in Histopathological Images Using Support Vector Machines, Naïve-Bayes, and K-Nearest Neighbor Classifiers," A. *Tallón-Ballesteros and C.-H. Chen, Eds. Netherlands: IOS Press BV*, 2020, 46–53.

[11] Magboo, V.P.C., and Ma. Sheila A. Magboo. (2021). "Machine Learning Classifiers on Breast Cancer Recurrences." *Procedia Computer Science*, **192** : 2742-2752. https://doi.org/10.1016/j.procs.2021.09.044

[12] Magboo, V.P.C., and Ma. Sheila A. Magboo. (2022). "Prediction Models for COVID-19 in Children." *In: Chen, YW., Tanaka, S., Howlett, R.J., Jain, L.C. (eds) Innovation in Medicine and Healthcare. Smart Innovation, Systems and Technologies*, **308**. Springer, Singapore. https://doi.org/10.1007/978-981-19-3440-7_2

[13] Seetharam, K., Shrestha, S., and Partho P. Sengupta. (2021). "Cardiovascular Imaging and Intervention Through the Lens of Artificial Intelligence." *Interventional Cardiology*, **2021 (16) :** e31. https://doi.org/10.15420/icr.2020.04

[14] Teuho, J., Schultz, J., Klén, R., Knuuti, J., Saraste, A., Ono, N., and Shigehiko Kanaya. (2022). "Classification of ischemia from myocardial polar maps in 15O–H2O cardiac perfusion imaging using a convolutional neural network." *Scientific Reports* **12 :** 2839. https://doi.org/10.1038/s41598-022-06604-x

[15] Mostafapour, S., Gholamiankhah, F., Maroufpour, S., et al. (2022). " Deep learning-guided attenuation correction in the image domain for myocardial perfusion SPECT imaging." *Journal of Computational Design and Engineering*, **9 (2) :** 434–447, https://doi.org/10.1093/jcde/qwac008

[16] Papandrianos, N.I., Feleki, A., and Elpiniki I. Papageorgiou, E.I. (2021) "Exploring Classification of SPECT MPI images applying convolutional neural networks." *In 25th Pan-Hellenic Conference on Informatics (PCI 2021), November 26–28, 2021, Volos, Greece. Association of Computing Machinery*, New York, NY, USA. https://doi.org/10.1145/3503823.3503911

[17] Chen, J.J., Su, T.Y., Chen, W.S., Chang, Y.H., and Henry Horng-Shing Lu. (2021) "Convolutional Neural Network in the Evaluation of Myocardial Ischemia from CZT SPECT Myocardial Perfusion Imaging: Comparison to Automated Quantification." *Applied Sciences* **11 (2)** : 514. https://doi.org/10.3390/app11020514

[18] de Souza Filho EM, Fernandes FdA, Wiefels C, et al. (2021) "Machine Learning Algorithms to Distinguish Myocardial Perfusion SPECT Polar Maps." *Frontiers in Cardiovascular Medicine*. **8** : 741667. https://www.frontiersin.org/articles/10.3389/fcvm.2021.741667

[19] Kikuchi, A., Wada, N., Kawakami, T., Nakajima, K., and Hiroto Yoneyama. (2022) "A myocardial extraction method using deep learning for 99mTc myocardial perfusion SPECT images: A basic study to reduce the effects of extra-myocardial activity." *Computers in Biology and Medicine*. **141** :105164. https://doi.org/10.1016/j.compbiomed.2021.105164

[20] Liu, H., Wu, J., Miller, E.J., Liu, C., Yaqiang, Liu, and Yi-Hwa Liu. (2021). "Diagnostic accuracy of stress-only myocardial perfusion SPECT improved by deep learning." *European Journal of Nuclear Medicine and Molecular Imaging*. **48** : 2793–2800. https://doi.org/10.1007/s00259-021-05202-9

[21] Poongodi, M., Hamdi, M., Malviya, M., Sharma, A., Dhiman, G., and S. Vimal. (2022). "Diagnosis and combating COVID-19 using wearable Oura smart ring with deep learning methods." *Personal and ubiquitous computing*, **26(1):** 25–35. https://doi.org/10.1007/s00779-021-01541-4

[22] Shabaz, M., Sharma, A., Al Ajrawi, S., and Vania Vieira Estrela. (2022). “Multimedia-based emerging technologies and data analytics for Neuroscience as a Service (NaaS).” *Neuroscience Informatics*, **2 (3)** : 100067. https://doi.org/10.1016/j.neuri.2022.100067

[23] SPECT-MPI dataset, Department of Nuclear Medicine, Eskisehir Osmangazi University from December 2018 to September 2019 for stress/rest Tc-99 m MPI. https://www.kaggle.com/selcankaplan/spect-mpi, last accessed 2022/2/28.

[24] Papandrianos, N., Papageorgiou, E., Anagnostis, A., and Anna Feleki, A. (2020). “A Deep-Learning Approach for Diagnosis of Metastatic Breast Cancer in Bones from Whole-Body Scans.” *Applied Sciences*, **10 (3)** : 997. https://doi.org/10.3390/app10030997

[25] Papandrianos, N., Papageorgiou, E., Anagnostis, A., and Konstantinos Papageorgiou. (2020). “Efficient Bone Metastasis Diagnosis in Bone Scintigraphy Using a Fast Convolutional Neural Network Architecture.” *Diagnostics*, **10 (8)** : 532. https://doi.org/10.3390/diagnostics10080532

[26] Hassan, M., Ali, S., Alquhayz, H., and Khushbakht Safdar. (2020). “Developing intelligent medical image modality classification system using deep transfer learning and LDA.” *Sci Rep* **10 :** 12868. https://doi.org/10.1038/s41598-020-69813-2

[27] Elpeltagy, M., and Hany Sallam. (2021). “Automatic prediction of COVID- 19 from chest images using modified ResNet50.” *Multimedia tools and applications*, **80** : 26451–26463. https://doi.org/10.1007/s11042-021-10783-6

[28] Yang, D., Martinez, C., Visuña, L., Khandhar, H., Bhatt, C., and Jesus Carretero. (2021). “Detection and analysis of COVID-19 in medical images using deep learning techniques.” *Sci Rep* **11** : 19638. https://doi.org/10.1038/s41598-021-99015-3

[29] Gaur, L., Bhatia, U., Jhanjhi, N.Z., Muhammad, G., and Mehedi Masud. (2021). “Medical image-based detection of COVID-19 using Deep Convolution Neural Networks.” *Multimedia Systems*. **2021**. https://doi.org/10.1007/s00530-021-00794-6

[30] Shazia, A., Xuan, T.Z., Chuah, J.H., Usman, J., Qian, P., and Khin Wee Lai. (2021). “A comparative study of multiple neural network for detection of COVID-19 on chest X-ray.” *EURASIP J. Adv. Signal Process.* **50 (2021)**. https://doi.org/10.1186/s13634-021-00755-1

[31] Hasan, N., Bao, Y., Shawon, A., and Yanmei Huang. (2021). “DenseNet Convolutional Neural Networks Application for Predicting COVID-19 Using CT Image.” *SN COMPUT. SCI*, **2** : 389. https://doi.org/10.1007/s42979-021-00782-7

[32] Kim, H.E., Cosa-Linan, A., Santhanam, N., Jannesari M., Maros, M., and Thomas Ganslandt. (2022) “Transfer learning for medical image classification: a literature review.” *BMC Med Imaging* **22 : 69**. https://doi.org/10.1186/s12880-022-00793-7

[33] Rastogi, P., Khanna, K., and Vijendra Singh. (2022). “LeuFeatx: Deep learning–based feature extractor for the diagnosis of acute leukemia from microscopic images of peripheral blood smear.” *Comput. Biol. Med*. **142** : 105326. https://doi.org/10.1016/j.compbiomed.2022.105236

[34] Rastogi, P., Singh, V., and Monica Yadav. (2018). “Deep Learning and Big DataTechnologies in Medical Image Analysis.” *2018 Fifth International Conference on Parallel, Distributed and Grid Computing (PDGC)*, **2018** : 60-63, doi: 10.1109/PDGC.2018.8745750

[35] Chen, X., Li, L., Sharma, A., Dhiman, G., and S Vimal. (2022). “The Application of Convolutional Neural Network Model in Diagnosis and Nursing of MR Imaging in Alzheimer's Disease.” *Interdiscip Sci Comput Life Sci*, **14(1):**34–44. https://doi.org/10.1007/s12539-021-00450-7

[36] Dhiman, G., Vinoth Kumar, V., Kaur, A., and Ashutosh Sharma. (2021) “DON: Deep Learning and Optimization-Based Framework for Detection of Novel Coronavirus Disease Using X-ray Images.” *Interdiscip Sci Comput Life Sci* **13** : 260–272. https://doi.org/10.1007/s12539-021-00418-7

[37] Singh, V., Asari, V.K., and Rajkumar Rajasekaran. (2022). “ Deep Neural Network for Early Detection and Prediction of Chronic Kidney Disease.” *Diagnostics*, **12 (1)** : 116. https://doi.org/10.3390/diagnostics12010116

[38] Otaki, Y., Singh, A., Kavanagh, P., et al. (2022) “Clinical Deployment of Explainable Artificial Intelligence of SPECT for Diagnosis of Coronary Artery Disease.” *J Am Coll Cardiol Img*., **15 (6)** : 1091–1102. https://doi.org/10.1016/j.jcmg.2021.04.030

[39] Apostolopoulos, I. D., Papathanasiou, N. D., Spyridonidis, T., and Dimitris J. Apostolopoulos. (2020). “Automatic characterization of myocardial perfusion imaging polar maps employing deep learning and data augmentation.” *Hellenic journal of nuclear medicine*, **23 (2) :** 125 – 132. https://doi.org/10.1967/s002449912101