Multi-classification of alzheimer disease on magnetic resonance images (MRI) using deep convolutional neural network (DCNN) approaches

Sunday Adeola Ajagbe\textsuperscript{1,}\textsuperscript{*}, Kamorudeen A. Amuda\textsuperscript{2}, Matthew A. Oladipupo\textsuperscript{3}, Oluwaseyi F. AFE\textsuperscript{4} and Kikelomo I. Okesola\textsuperscript{4}

Ladoke Akintola University of Technology, LAUTECH, Ogbomoso, Nigeria\textsuperscript{1}
University of Ibadan, Ibadan, Nigeria\textsuperscript{2}
University of Salford, Salford, Greater Manchester, United Kingdom\textsuperscript{3}
Lead City University, LCU, Ibadan, Nigeria\textsuperscript{4}

Received: 01-February-2021; Revised: 29-March-2021; Accepted: 30-March-2021
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Abstract
Alzheimer's disease (AD) is the most popular cause of dementia. Dementia refers to a continuous decline in mental ability. The developmental stages of this neuropsychiatric symptom are usually examined using medical images of the brain. Cutting edge technologies, including computer algorithms have been applied to the diagnosis and treatments of AD, especially in the area of detection and classification. These technologies have eased up the work of medical experts and provided faster ways of medical delivery. This study was aimed at advancing AD image classification with deep convolutional neural network (DCNN) involving convolutional neural network (CNN) and transfer learning (Visual Geometry Group (VGG)16 and VGG19) using magnetic resonance images (MRI) and extend the evaluation metrics since limitations and capacity of algorithms cannot be revealed by few metrics. The objectives of this research are to classify AD images into four known classes by neurologists and results of the finding are subjected to many evaluation metrics. This research used computer algorithms majorly DCNN and transfer learning to classify AD. Six metrics were used for the evaluation; accuracy, area under curve (AUC), F1- score, precision, recall and computational time. VGG-19 was the best in three, CNN was the best in two and VGG-16 was the best in one. Conclusively, this study has proven that computer algorithms are capable of classifying AD into four classes known to medical experts.

Keywords
Alzheimers disease, Deep learning, Image classification, Medical images, Magnetic resonance images, Deep Convolutional neural network.

1. Introduction
Medical issues have become the most popular issues in the world, and both the medical experts and researchers are working tirelessly at advancing medical diagnosis, treatments and examinations in order to save human lives and enhance healthy living. One of the medical issues that is challenging human health is AD. Alzheimer disease and vascular dementia are common brain diseases. Dementia is a neurodegenerative brain disorder that is characterized by the continuous loss of cognitive functions [1, 2]. AD has no cure for now, and it is considered destructive to human health and healthy living. It has affected many people around the world.

Therefore, early diagnosis of this disease with computer-aided tools is among research interest and highly imperative for both medical and computer science and engineers [3]. Classification of images is an important part of image analysis, computer vision and pattern recognition. It is the process of assigning one or more labels to an image. Traditional image classification is characterized with low-level and mid-level features extraction to present the image and a trainable classifier used for labelled dataset. DCNN has a high-level of feature extraction that made it to be superior to other feature extraction methods. Both feature extraction and classification networks are combined together and trained end-to-end in DCNN. Deep learning techniques were also being applied to medical image classification and computer-aided diagnosis tools. Wang et al. [4], introduced fundamentals of DCNN for image classifications first.
and then introduced an application of deep learning to the classification of focal liver lesions on multi-phase CT modality. Challenge in deep-learning medical image classification was identified to be a lack of annotated training data sample, fine-tuning was demonstrated for improved accuracy of liver lesion classification, particularly in small dataset.

DCNN and machine learning approaches are members of the same family, but DCNN has proven to have potential for different tasks including classifications. Notably, convolutional neural network (CNN) has the best results on various tasks in image classifications. Invariably, medical image data are very difficult to be assessed because it needs a lot of expertise to label them. CNN and transfer learning algorithms were applied to chest images of X-ray modality to classify pneumonia. Three techniques were experimented and evaluated. Support vector machine (SVM) classifier was used with local rotation and orientation free features, two transfer learning models: Inception V3 and visual geometry group (VGG 16) were also used. Data augmentation was done as part of data preprocessing techniques. The results of the experiments show that transfer learning were better classification techniques on a small dataset compared to SVM [5].

Alzheimer’s disease has atrophy of the cerebral cortex compared to the cerebral cortex in normal brain. This disease has an enlarged ventricle compared to the ventricles in normal brain. It has atrophy of the hippocampus compared to the hippocampus in normal brain. Meanwhile, normal brain has Gyrus and Sulcus that AD is lacking. Previous studies, including Jain et al. [3] have classified AD, but no studies have considered using computer-aided tools for analysis AD through its developmental stages to prevent the growth and further damages that the disease will consequently cause to human health. There are developmental stages which are classified into Mild demented, Moderate demented, Non-demented (normal brain) and Very mild demented (mature stage of Alzheimer’s disease). Although, computer aided devices and algorithms such as CNN, VGG 16, VGG 19, ResNet50, GoogLeNet, AlexNet have been used for medical image classifications with different image modalities, but none of these algorithms have been used to classify Alzheimer’s disease up to four known categories. Therefore, the first objective of this research is to classify AD into four known stages of development. Second is to carry out empirical analysis of AD multiple classifications using deep convolutional neural network (DCNN) and transfer learnings such as VGG 16 and VGG 19 algorithms. Third is to evaluate the performance of classification algorithms using different evaluation metrics.

2. Review of related works

Images are one of the data expression methods in photography form. It consists of small elements called pixels that have a specific value and position. The techniques of handling an image using computer algorithms are known as Image Processing. Image processing is an important part of the many image analysis. Indeed, the model proposed for image processing defines the requirements for compression, coding, denoising, contrast enhancement, classification, feature extraction and other image processing activities [6]. It is applicable in many fields including medicine, and used in medical image classification, segmentation, and analysis. Medical imaging modality system includes, but not limited to X-ray imaging system, magnetic resonance imaging, ultrasound, computed tomography and nuclear medicine [7]. The development in medical imaging is rapid, because of innovations in image processing techniques which includes pattern recognition, image enhancement and analysis. These innovations raised the amount and percentage of tissues detections in medical images. Both sophisticated and simple medical image processing techniques were presented, using different image processing algorithms like ROI-based segmentation, watershed techniques and k-means [7].

Deep learning area of research focuses on image processing [8], and medical image classification is an interesting and challenging research area in computer vision, biomedical engineering, computer science and engineering generally but specifically imaging applications. Classification of medical images is done with respect to image characteristics and in line with the issue at hand. [9, 10]. The characteristics and quality of medical images are affected by noise [11]. Thus, denoising or noise removal of digital image has to be done to improve the quality of images as it affects post processing and analysis during image classification, segmentation and pattern recognition [11, 12].

Recent findings, including Sahinbas and Catak [13] (2020) revealed that the application of X-ray and magnetic resonance images can help in the accurate classification and detection of diseases. The study proposed a COVID-19 detection model and applied DCNN model using preprocessed COVID-19
patients’ chest X-ray images, 50 each for positive and negative cases as training dataset and 20 each for positive and negative cases as testing dataset. Since the classification of X-ray images need deep architecture to deal with the complicated structure of images. Five different models of deep CNN were applied, namely; VGG16, VGG19, DenseNet, InceptionV3 and ResNet. The study achieved highest classification accuracy of 80% among the proposed approaches using a limited COVID-19 dataset.

Sharma, et al. [14] developed a software to achieve auto classification and segmentation of medical images through tissue characterization. Initial algorithms were seen to be designed and developed for medical image analysis based on statistical and hybridization of syntactic algorithm with artificial neural network (ANN). The model performed classification and segmentations is being done by human experts, that recognizes surface incline by texture information and object; brightness and perceives depth; identifies different textures, curved surfaces.

Sharma, et al. [15] noted and presented a direct combination of the following steps of image processing: segmentation, feature extraction and extracted features analysis by classifier or pattern recognition system as one step. It was a semi supervised approach because the definition of the texture-primitive cell; algorithm, it scans the whole image and performs the classification and segmentation in unsupervised mode. Markov textures were used to test the algorithm and 100% classification was achieved. The algorithm was later used to test an impregnated image with distorted Markov texture cell and work well. The algorithm was applied to medical images selection for classification and segmentation purposes. Results were similar to the clinician segmentation, but it has not been used for multiple classifications like this study.

Convolutional neural network was used in classifying and identifying objects in a real time video from a study by Sharma et al. [14]. The research used the popular DCNN such as GoogleNet, AlexNet and ResNet 50, and popular video dataset such as CIFAR10, CIFAR100 and imagine were used to test the performance of each algorithm on a different dataset. The results showed that ResNet 50 and GoogleNet were able to recognise objects with better precision than AlexNet. Talo[16] (2019) noted the need to improve medical diagnosis quality and reduce time to analyze histopathology image processing through automated system. Automated classification and detection of pathological tissue characteristics with computer-aided devices are a critical step in early diagnosis and treatment in medicine. The ResNet-50 and DenseNet-161 pre-trained CNN models have been used to classify digital histopathology images via transfer learning algorithm. The models proposed were tested on color histopathology and grayscale images. The ResNet-50 model achieves 98.87% accuracy for color images and DenseNet-161 model achieved 97.89% accuracy using grayscale images.

In another study by Marghalani and Arif [17] (2019) image processing methods and computer vision (CV) was proposed as an intelligent system for classification and detection of brain pathologies like tumors, normal brain or AD images. The algorithm proposed consist of 4 stages: MRI modality was used for acquisition of images, image preprocessing, feature extraction, and classification were done. The study classified images using a bag of features module for MRI acquired data set. The images were classified into the brain with a tumor and normal brain MRI on a binary classification. The model achieves 97% accurate, but other metrics were not considered; and the image classification in the study was just two.

Image classification plays an important part in the field of medicine and teaching research. Radiologists and medical experts see tumor detection and extraction as such a tedious and arduous task to perform. The analysis and accuracy depend on their experience alone. However, there is a limit to consistent analysis and accuracy of both experienced and inexperienced medical expert. In fact, the task becomes increasingly burdensome when there are abundant data present to be analyzed. Hence, the use of cutting-edge technology comes in hand to overcome these challenges.

Seetha and Raja [18] came up with a method for brain tumor in two-dimensional magnetic resonance images (MRI) using Convolutional Neural Network, implemented using Keras. The real-time dataset was used for the experiment, having images with varied tumor factors like image shape, intensity and size. Meanwhile, the aim of the study was to classify the MRI images into benign and malignant brain tissues which is just a two-way classification. The study achieved 95% accuracy in the results, the
effectiveness of the proposed technique was demonstrated on a single performance metrics.

Amini and Rabbani [6] worked on the classification of the models used in medical image processing. A wider categorization was done, each model was applied in transforming or spatial domain. Transform domain algorithm was also divided into two based on the choice of basis function as adaptive data and non-adaptive data transform models. Aside from classification, both the transform and spatial domain models were also categorized into either stochastic, deterministic, partial differential equation (PDE) or geometric based models. An attempt was made to work on and around classification of different models used for medical images, but it was noted that these models were not entirely different from each other and in many cases; they have overlap characteristics. Furthermore, two examples on optical coherence tomography (OCT) and colour fundus image processing applications were presented. It was concluded that the study will be beneficial to researchers in a model cognitive selection for their own specified project.

The high dimensionality of the datasets was seen as a challenge for domain engineer and researchers to achieve their goal of generating heterogenous data on world wide web (www) through the machine learning (ML) models selected in a study by Iqbal et al. [19] ML plays a significant role in selecting most relevant features of high dimension dataset, especially images and improve the performance of the training dataset in the model. It also features selection process that provides an effective way of eliminating redundancy in the dataset and ultimately shrinks the computational time. Feature selection is very important for effective spam detection systems, management of documents, information retrieval and pattern recognition systems. Iqbal et al. [19] carried out an overview of text classification by survey. The study covered popular feature selection models used for text classification and explained applications of feature selection models. The study featured three data selection algorithms, namely: Chi-Square (CS), Principal Component Analysis (PCA) and Information Gain (IG). An experiment was conducted using web spam uk2007 dataset. Ten, twenty, thirty, and forty features were selected as an optimal subset from web spam uk2007 data. CS and IG achieved highest F1Score of 0.911 among the selected algorithms, but took longer time to build the models. This study provides useful information for researchers searching for some suitable technique to be used for classification project.

Performance metrics for medical images was noted as a major problem in the classification of medical dataset. Previous studies, including [20, 21] using several examples, it was revealed that imbalance can exert serious impact on the accuracy and value as well as certain other well-known metrics. Luque et al. [22] proposed approach that goes beyond the simple study case and develops a systematic analysis of the impact by simulating the results obtained using binary classifiers. A set of numerical indicators and functions were attained that enables the comparison of the behaviour of several performance metrics based on the binary confusion matrix when they were faced with imbalanced datasets. The result of the simulation shows several clusters of performance metrics that were identified involving in the use of Bookmaker Informedness or Geometric Mean as the best null-biased metrics when focusing on classification successes revealed. It was concluded that using several metrics to analyze models will reveal the limitation and strengths of the models better than few metrics. Hence, the three models (CNN, VGG-16 and VGG-19) used in this study will be evaluated on six common image analysis metrics.

2.1 Convolutional neural networks (CNN)
Convolutional neural networks and deep learning generally have been contributing immensely to various innovations such as image classifications and segmentation, as well as object detection and recognition research on computer vision [23]. Deep learning techniques have been successfully implemented in automation task and eliminating the tedious work of handcrafted engineering gradually. CNN and deep learning were trying to mimic the human visual cortex system in structure and operation by adopting a hierarchical layer of feature representation. Multilayer CNN model it possible to train different image features automatically, and enabled CNNs to perform better than hand crafted-feature techniques [24].

2.2 VGG.Net model
VGG models have a very small convolutional network and was developed by Simonyan and Zisserman [25] It is a simple model, but significantly different from previous models. It has more in-depth structure and is followed by double or triple convolution layers compared to previous models where the sharing layers and convolution follow each other. It is basically of models, VGG-16 and VGG-
19. The architecture of VGG-16 has 16 convolutional layers out of which 13 are being used for feature extraction and 3 for filtering, and each convolution layer has a ReLU layer and maximum pooling layers for sampling. Three of its layers are fully for classification, out of which two serves as hidden layers, and the third for the classification layer that comprises 1000 units representing image categories in the ImageNet database.

This structure simulates a larger filter while preserving the benefits of smaller filter sizes. It has shown to perform better when using fewer parameters, compared to previous models. Furthermore, two ReLU layers were used instead of a single ReLU layer for two convolution layers. It works effectively for both object classification and edge detection problems, and these features informed its choice in this study [13].

Significance of image classification in the field of medicine is exceptional, as it aids diagnosis and treatment of patients and also ease the work of the medical experts. Medical image classification is gaining a growing attention from both the medical experts and research community. It supports analysis of medical images and enhance teaching and research purposes in the medical field [26]. Image modalities and application based on data mining methods have been proposed and developed, but most of these works focused on accuracy of medical image classified with few attentions on other performance metrics that can assist clinicians in early diagnosis of AD and learning how the disease progressed. Hence, multi-classification of medical image for AD/dementia patients were proposed in this research. Although, it is worthy of note, that the reviewed literatures shows a significant improvements in using computer aided devices and algorithms (CNN, VGG 16, VGG 19, ResNet50, GoogLeNet, AlexNet) for medical image classifications, and it reduces time and efforts expended on manual classifications, but none of these algorithms has been used to classify AD up to four known categories. Hence, there is need to advance the scope of study in medical image processing beyond the present state by experimenting the four classes of AD with DCNN approaches and analyze their performances using different evaluation metrics, since the limitations and capacities of algorithms cannot be revealed by few evaluation metrics.

3. Methods and materials

The procedure and the materials used in this research are contained in this section. This includes the (image) data acquisition, Image Preprocessing, Model building, Soft set Classification, and Evaluation of models. Figure 1 depicts the block diagram of the proposed methodology for multi-classification of Alzheimer’s disease, the operation that took place in each of the procedures are directly under each of the procedures as showed in the block diagram.

![Figure 1 Block diagram of the proposed methodology for multi-classification of Alzheimer’s disease](image)

### 3.1 Image data acquisition

An online dataset was acquired from Kaggle® for this research, specifically www.kaggle.com/tourist55/alzheimers-dataset-4-class-of-images, Kaggle® provide a reliable online dataset for research and analyses in many areas.

Dataset acquired contained 6400, and it was partitioned as follows: Train set with 4098 images and four classes, Test sets with 1279 images and four classes, Validation set with 1023 images and four classes. The four classes of AD developmental stages are Mild demented, Moderate demented, Non-
demented (normal brain) and Very mild demented (mature stage of Alzheimer’s disease).

3.2 Image preprocessing
In preparing the image medical data for this study, ImageDataGenerator class provided by Keras was used to perform the following ways:
- Images were formatted to appropriately pre-processed floating-point tensors before sending to the model, so that images can be read easily from the disk.
- The contents of the images were decoded and converted into grid format as per their RGB content, and convert the image data to floating point tensors.
- Image random flipping and image random zooming were done.
- Images were rescaled in tensors from values between 0 and 255 with values between 0 and 1.
- Then generator was set up to convert images in batches of the tensor to train the model.

3.3 Model building
The deep convolutional neural network (DCNN) models built for experimentation in this study are convolutional neural network, VGG 16 and VGG19. In building the models, particular attentions were paid to:
- Epoch as is a single step in a training neural network and evaluation.
- Categorical Cross Entropy as a form of cross entropy loss or log loss that is used to measure the performance of a multi-classification problem whose output is more than two (softmax)
- Batch size as it described the number of samples to work through before updating the internal model parameters.

3.4 Image classification
Three models built in this study were used to classify AD (medical images) into four classes of AD developmental stages with Mild demented, Moderate demented, Non-demented (normal brain) and Very mild demented (mature stage of Alzheimer’s disease). Hyperparameters such as dropout value was used to partition the dataset into training set and test set, dropout and other hyperparameters such as learning rate, activation function, number of hidden layers in the networks, epoch, cross entropy and batch size were all adjusted to tune the neural network so that it can train the models properly for accurate classification of the dataset. The generators were defined for training and image validation, the flow_from_directory techniques to load images from the disk, rescaling, and resizes the images were applied to achieve required dimensions.

3.5 Evaluation
The dataset used for this study was almost balanced. However, the traditional accuracy and evaluations are subjective in finding out performance of classification models in this scenario. Six performance metrics were used to evaluate the models in this research, while numerous and relevant evaluation performance metrics were used to analyze the limitations and capacities of the selected models, namely; Accuracy rate, Area Under Curve, F1-Score, Precision, Recall and computation time.

4. Implementation and results analysis
This section described the implementation of this research, including the execution environment, presentation, discussion and analysis of the results.

4.1 Implementation
This study was implemented using some software and hardware specifications, which are keen to the implementation and results of this study.

4.1.1 Software requirements
The following programming software packages were installed on the machine/laptop for the successful implementations of this research. The system software was Window 10 with 64-bit Operating System (OS) and the following Python programming application packages/libraries were installed/imported; Anaconda, Jupyter notebook, Matplotlib was the use of data visualization, TensorFlow and Keras were used to develop the models for classification, sklearn metric was used to measure the performance of the models.

4.1.2 Hardware requirements
The hardware configuration of the computer system used are; HP Elite Book Folio 9480m, Intel Core i7 4600U Processor, 8GB RAM, 14 Inch Full HD Screen, 256GB SSD.

4.2 Results
The graphical Visualization results of the three DCNN considered in this research were shown in Figure 2, 3 and 4 for simple CNN, VGG-16 and VGG-19 respectively. The performance of AD image classification of five metrics namely; accuracy rate, area under curve, F1-score, precision and recall were visualized, but computation time could not be visualize alongside others because they were not in the same units. However, Figure 5 presents the results of the six evaluation performance metrics of multi-classification; accuracy rate, area under curve,
F1-score, precision, recall and computational time in the histogram. Evaluation results are presented in Table 1.

Figure 2 Graphical visualization of CNN performance on Alzheimer’s disease image multi-classification

Figure 3 Graphical visualization of VGG-16 performance on Alzheimer’s disease image multi-classification

Figure 4 Graphical visualization of VGG-19 performance on Alzheimer’s disease image multi-classification
Table 1 Evaluation results

| Evaluation metrics | Model performances |
|--------------------|--------------------|
|                    | CNN                | VGG-16             | VGG-19             |
| Accuracy (%)       | 0.7102             | 0.7704             | 0.7766             |
| AUC (%)            | 0.7806             | 0.8122             | 0.8155             |
| F1_Score (%)       | 0.5004             | 0.4617             | 0.4505             |
| Precision (%)      | 0.5004             | 0.5708             | 0.5848             |
| Recall (%)         | 0.5004             | 0.3878             | 0.3667             |
| Computation time (hours) | 0.8600 | 2.6200 | 3.7600 |

Figure 5 Bar chat for Alzheimer’s disease image multi-classification models performance

5. Discussion
The experiment was evaluated using six different metrics in order to ascertain the performance of the models. The following performance metrics were used namely; accuracy, area under curve (AUC), F1-score, precision, recall and computational time. Among the three models experimented, VGG-19 achieved better performance by having 0.7766(%), 0.8155(%) and 0.5848(%) in accuracy, area under curve and precision respectively. It was closely followed by VGG-16 while basic CNN has the least performance. However, CNN performed better than VGG-16 and VGG-19 having achieved 0.5004(%) each in both F1_score and recall and followed by VGG-19 while VGG-16 has the least performance. CNN also achieved lowest computation time of 0.86 hours, followed by 2.62 hours by VGG-16 and 3.76 hours by VGG-19. The accuracy here seems to be lower compared to Marghalani and Arif [17] that did a similar study and achieved 97%, but considered only three classes while this study considered four classifications of Alzheimer’s disease. In all, this research showed outstanding performance since AUC of three models are beyond 0.5, and it has extended medical image processing beyond previous research by [16, 18, 22, 27].

5.1 Limitations
Unavailability of real-life or local dataset for the experiment was part of the limitation of this research and the machine for the implementation showed that there was a high computational time, these might have impacts on the results of this research.

6. Conclusions and recommendations
This research has presented multi-classification of Alzheimer’s disease with CNN, VGG16 and VGG19 and proved that deep convolutional neural network approaches is possible for multiple classifications of medical images which can be applied to medical image classification. This study applied these algorithms (CNN, VGG-16 and VGG-19) to carry out medical image multi-classification of AD dataset, and the results of the multiple medical image classification was good though, there is room for improvement. VGG-19 achieved best performance in accuracy, area under curve and precision, it was closely followed by VGG-16 while basic CNN has lower performance. However, CNN performed better than VGG-16 and VGG-19 both in F1, recall and computation time VGG-19 while VGG-16. This research has also advanced medical image processing by using numerous and relevant evaluation metrics, to reveal the limitations and capacities of the models.
This research will help the neuropsychiatric and other medical experts in making correct decisions as regards the correct stages of AD since classification help decision making.

The following may be considered in future research;
1. Other architectures of the Deep Convolutional Neural Network such as GoogLeNet, ResNet, AlexNet, CapsuleNet should be used for multiple classification of medical images.
2. High computing power like GPU, TPU processor are advisable to be used for this kind of research. For instance, the training time on the CPU is slower with approximately 3hours.
3. The real-life dataset should be used instead of using dataset from public repository such as Kaggle, UCI, Google and others.

Acknowledgment

None.

Conflicts of interest
The authors have no conflicts of interest to declare.

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Sunday Adeola Ajagbe is an MPhil/PhD candidate of Computer Engineering at Ladoke Akintola University of Technology (LAUTECH), Ogbomoso, Nigeria. He obtained MSc and BSc in Information Technology and Communication Technology respectively at National Open University of Nigeria (NOUN), and his Postgraduate Diploma in Electronics and Electrical Engineering at LAUTECH. His specialization includes Natural language Processing, Signal Processing, Information Security, Quantum Computing, Artificial Intelligence, Deep Learning and Machine Learning, Smart Solution and Biomedical Engineering. He has successfully carried out researches and published many articles. He is a member of many academic/professional bodies including Nigeria Computer Society among others.
Email: saajabe@pgschool.lautech.edu.ng

Kamorudeen AMUDA holds a BSc (Ed.) in Computer Science from Adekunle Ajasin University, Ondo State and MSc in Computer Science with a specialization in Data Mining and Analytics from the University of Ibadan, Nigeria. Currently, he is a fellow of Fatima Al-fihri Predoctoral Fellowship, United State of America and also he is a member of Institute of Electrical and Electronics Engineers (IEEE), International Association of Engineers (IAENG), Association of Computing Machinery (ACM) and Internet Society (ISOC) His research interests are Data Mining, Machine Learning, Deep Learning and Artificial Intelligence.
Email: akindeleamuda@gmail.com

Matthew Abiola Oladipupo is a Data Scientist with his area of specialization in Big Data, Advanced Database System (DBMS), NLP, Machine Learning, and Deep Learning. He is currently pursuing his MSc in Data Science at the University of Salford, Manchester, UK. He obtained both his BTech and PGD in Electronic Electrical Engineering from Ladoke Akintola University of Technology, Ogbomoso, Nigeria. He is a member of the Nigerian Society of Engineers (NSE), Institute of Electrical and Electronics Engineers (IEEE), International Association of Engineers (IAENG), Association of Computing Machinery (ACM) Data Science Nigeria (DSN), and also licensed by The Council Regulating Engineering in Nigeria (COREN) as a professional Electrical Engineer. He is currently working on Hadoop Mapreduce, Hadoop Hive, RDDs, Spark Dataframe, Spark SQL.
Email: m.a.oldapupo@edu.salford.ac.uk

Oluwaseyi F. AFE is from the Department of Computer Science, Lead City University, Ibadan, Nigeria. She is currently on her PhD at the University of Ibadan, where she also obtained her MSc in Computer Science. Her research interest focuses on Computer Vision, Pattern Recognition, and Digital Image Forensics, a PhD Computer Science candidate at University of Ibadan.
Email: afe.seyi@lcu.edu.ng

Kikelomo I. Okesola is from the Department of Computer Science, Lead City University, Ibadan, Nigeria. She is currently a PhD candidate at the University of Ibadan, Nigeria where she also obtained her MSc. Her research interest is in knowledge management, artificial intelligence, NLP and Image processing.
Email: kikelomo.okesola@lcu.edu.ng