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Computer Aided Diagnosis System for Classification of Abnormalities in Thyroid Nodules Ultrasound Images using Deep Learning

Oluwadare Adepeju Adebisi[1],John Adedapo Ojo[2], Temitope Olugbenga Bello[3]
[1]*(Departmentof Computer Engineering,The Polytechnic Ibadan, Nigeria)*
[2]*(Professor of Communication & Signal Processing, Department of Electronic and Electrical Engineering, LadokeAkintola University of Technology Ogbomoso, Nigeria)*
[3]*(Professor of Radiology, Department of Radiology, LadokeAkintola University of Technology Teaching Hospital Osogbo, Nigeria)*

Abstract:*Thyroid nodules, which are abnormal cell growth that forms a lump in the thyroid gland occurs in more than 50% of the adult population. While ultrasonography is a commonly used for diagnosis because it is non-invasive, non-radioactive, relatively inexpensive and widely available, the usual visual interpretation results in subjective interpretation, inter-observer variability and it's a time-consuming process. In addition, different stages of malignancy may not be detected, even in existing Computer Aided Diagnosis (CAD) systems. Therefore, there is need for CAD systems that can classify thyroid nodules into multiple stages of malignancies. In this work, we developed a classification system that classifies ultrasonic thyroid images into Thyroid Imaging Reporting and Data System (TIRADS) classes using convolutional neural network. Histogram equalization and adaptive filtering were used to improve the image contrast and noise removal respectively, while transfer learning with Alexnet was used to classify into 6 TIRADS classes. The developed system achieved an overall performance of 92% accuracy, 91% sensitivity and 99% specificity. The work will provide a second opinion, aid early and more accurate detection, thereby enhance treatment and management procedures.*

Keywords: *Deep Learning, TIRADS, Computer aided diagnosis system, Transfer Learning, Convolutional Neural Network*

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I. Introduction

A thyroid is an endocrine gland that produces hormones, which help the body to control metabolism. It is a small butterfly shaped gland located in front of the neck below the thyroid cartilage (Adam's apple) [1]. Thyroid nodule refers to any abnormal growth that forms a lump in the thyroid gland [2]. Thyroid nodules can be present in any part of the gland and may be benign or malignant. Further classification of thyroid nodules is based on The Thyroid Imaging Reporting and Data System (TIRADS) score.

TIRADS are standardized thyroid risk stratification system for thyroid lesions, which is based on ultrasound characteristics. TIRADS classes are built on the risk of malignancy, which depends on the number of suspicious ultrasound features [3]. The TIRADS classes are TIRADS 2 (benign conditions, 0% malignancy), TIRADS 3 (probably benign nodules, <5% malignancy), TIRADS 4a (one suspicious feature), TIRADS 4b (two suspicious features), TIRADS 4c (three or four suspicious features) and TIRADS 5 (five suspicious features >80% malignancy). The thyroid image features considered as suspicious are solid component, hypoechogenicity, microlobulated or irregular margins, microcalcifications and taller than wide. The common thyroid nodules diagnosis methods include Fine-Needle Aspiration (FNA) biopsy, excisional biopsy and thyroid nodule ultrasonography.

Fine-Needle Aspiration biopsy is a procedure that is used to test for cancer in thyroid nodule. In this method, a thin hollow needle is inserted into the mass for sampling of cells, which after being stained is examined under a microscope (biopsy). Although, Fine-Needle Aspiration is a safe procedure, it involves slight risk such as bleeding at biopsy site, infection and missing of problematic cells [4]. It has also been reported that about 10-20 percent of biopsy specimens are interpreted as inconclusive or inadequate therefore, the pathologist cannot be certain whether the nodule is cancerous or benign and may require excisional biopsy to make a decision [5].

Excisional biopsy is a medical procedure in which the entire thyroid nodule is removed for diagnosis. Excisional biopsy minimizes the chance of missing problematic cells during pathological examination. However, the diagnostic procedure is very labor intensive for large scale screenings and unnecessary biopsy will make patient anxious. Therefore, a non –invasive computer aided method is necessary for thyroid nodules diagnosis. Several medical imaging techniques such as X-ray, Computed Tomography (CT), Magnetic Resonance Imaging (MRI) and Ultrasound (US) have been used to assist in diagnosis of different diseases [6]. Ultrasonography is frequently used because it is non-invasive, without ionizing radiation and produce high resolution image. However, visual interpretation of ultrasound thyroid nodules images result in subjective interpretation, inter-observer variability and time consuming process. Only few experts are also available to interpret the images obtained.

CAD systems have been developed to assists radiologist in the interpretation of ultrasound thyroid nodules images and evaluate information obtained from medical imaging in short time for proper detection and diagnosis [7]. However, the existing CAD systems can only classify thyroid nodules into benign and malignant, which is not adequate for detailed evaluation of thyroid nodules. Therefore, there is need for CAD systems that can detect and classify thyroid nodules into multiple stages of malignancies to provide adequate information for proper assessment of thyroid nodules. Recent advancements in deep learning enhance multi-class image classification. Deep learning is a sub-field of machine learning in which a model learn features and tasks directly from data using neural network. Unlike other machine learning algorithms, it is capable of handling high dimensional data and efficient in focusing on the right features onits own [8].Deep Learning consists of multiple layers, which permits high level of abstraction and improved predictions of data. However, training deep neural network from scratch requires large number of labeled dataset, which are not usually available especially in medical field .The problem of large dataset is overcome by transfer learning.

Transfer learning is the process of fine tuning a deep neural network to classify a new collection of images [9]. Transfer learning is usually much faster and easier than training a new network. This is because learned features can be applied to a new task using a smaller number of training images. Transfer learning is usually achieved by pre-trained models. AlexNet is a pre-trained convolutional neural network developed by Krizhevsky*et al*. [10] and trained on more than one million images from the ImageNet database. As a result, the network has learned rich feature representations for a wide range of images. Alexnet won ImageNet Large Scale Visual Recognition Competition (ILSVR) in 2012 and achieved a winning top-5 with a test error rate of 15.3%. This paper aims to develop an efficient computer aided diagnosis system for classification of abnormalities in ultrasound thyroid nodules by modifying an Alexnet.

III. Methodology

3.1 Data Acquisition

Ninety nine (99) thyroid nodules images were obtained from The Computer Imaging and Medical Applications Laboratary (CIMLAB), which is a public open access dataset [19]. CIMLAB dataset is presented as a XML file with radiologist's annotation and diagnostic description of suspicious thyroid lesions. Radiologist's inference on each image was taken into consideration so as to be used as the basis for the evaluation of the system. The dataset hasbeen labeled and categorised into 6 TIRADS classes which are TIRADS 2 (benign conditions, 0% malignancy), TIRADS 3 (probably benign nodules, <5% malignancy), TIRADS 4a (one suspicious feature), TIRADS 4b (two suspicious features), TIRADS 4c (three or four suspicious features) and TIRADS 5 (>80% malignancy).

3.2 Preprocessing

Histogram Equalization was used to enhance the thyroid image contrast. The histogram shows the relative frequency of occurrences of pixel in a given image. The non-uniform changeable image due to external conditions is equalized to a uniform variation. The image noise was removed by using adaptive filtering technique and the resulting images were converted to binary by image binarization.

3.3 Classification of Thyroid Nodules using amodified Alexnet

Alexnet was retrained to classify thyroid nodules into six categories of malignancy. Training a model from scratch requires a lot of labeled training data and computing power (hundred gpu-hours or more).Alexnet is a convolutional neural network that was trained on more than a million images from the imagenetdatabase . The network consists of 8 covolutional layers and 227-by-227 image input size. The network has learned rich feature representations for a wide range of images and can classify images into 1000 object classes.

The Alexnet transfer learning network for thyroid nodules classification is shown in Figure 1. It consists of five convolutional layers and three fully connected layers. Each convolutional layer is followed by rectified linear units. A softmax layer was added after the final layer to classify the thyroid nodules and a max pooling layer was applied after each convolution layer to reduce the network size. Dropout was also applied to avoid overfitting by setting the output of each hidden neuron zero with probability of 0.5.

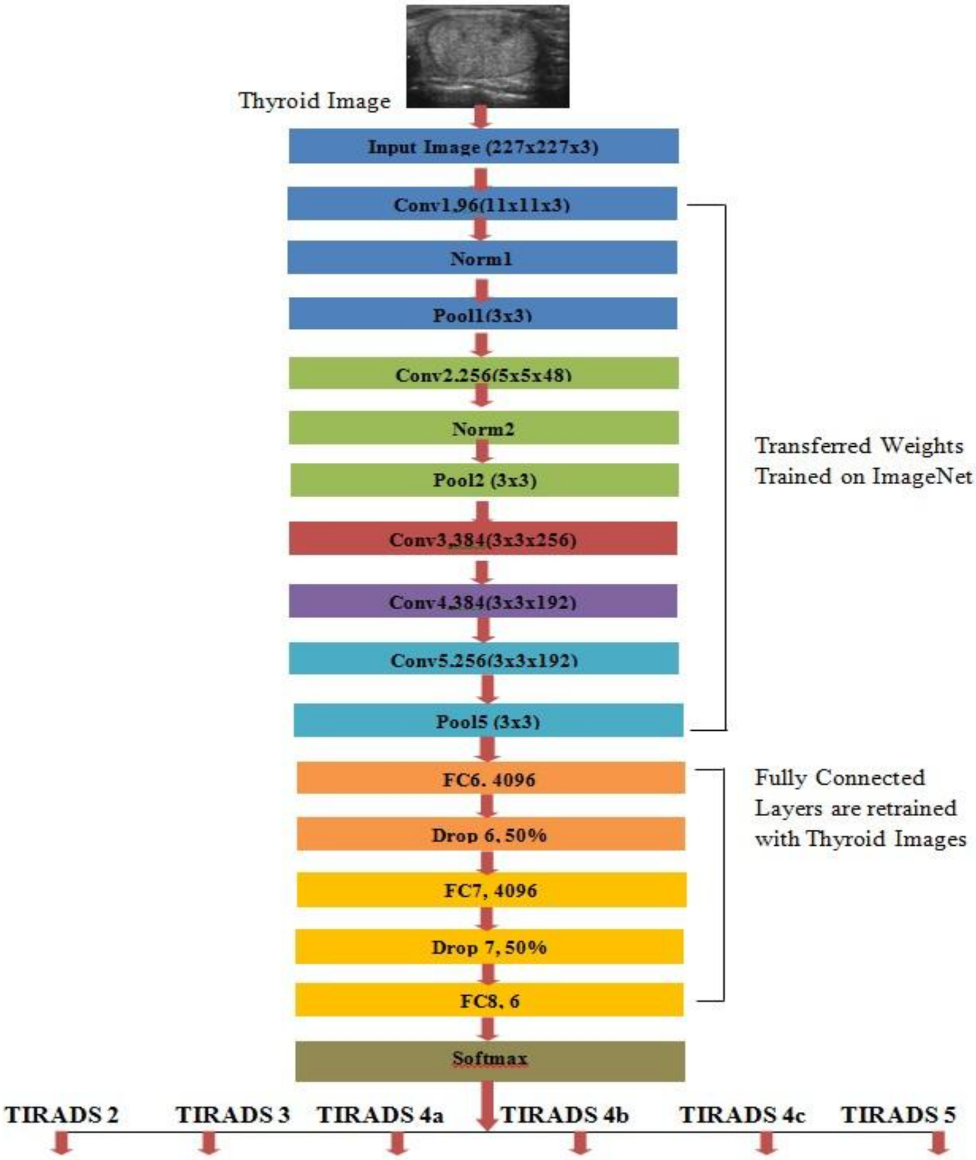

Figure 1 Alexnet transfer learning network for thyroid nodules classification

Figure 2 shows the flow diagram for the classification of thyroid nodules into 6 TIRADS classes by fine tuning the Alexnet network. The original size of the thyroid images obtained from CIMLAB was 346 × 307×1. Since the pretrainedalexnet network require the size of an input image to be the same as the input size of the network, each thyroid image size was changed to 227× 227×1. Furthermore, Alexnet requires 3-channels input data, therefore, the thyroid images were converted from grayscale to RGB (227 × 227 ×3) by concatenating their channel three times. Figure 3 shows the architecture of the modified Alexnet. The last three layers were replaced with new layers applied to thyroid nodules. The final fully connected layer (FC8) was disconnected in order to add a new layer having 6 output neurons, which corresponds to the number of Thyroid Imaging Reporting and Data System (TIRADS) classes of the thyroid nodules

In order to prevent overfitting that may be encountered during training, data augmentation was applied to increase the number of thyroid images obtained from CIMLAB database. Each thyroid image was rotated left and right and then flipped 70, 160 and 270 degrees, resulting to a total number of 1200 images (200 images in each TIRADS category). The training options were specified and the Alexnet was trained with training thyroid images. 70% of the CIMLAB dataset were used for training of the Alexnet while 30% were used for validation. Training options and network configuration were altered until the most impressive results were obtained. Thyroid images were classified into 6 TIRADS classes. The designed algorithm was implemented in MATLAB 2018 installed on a laptop computer system with an intel core processor i5, 2.8 central processing unit (CPU) processor speed, 8 GB of RAM.

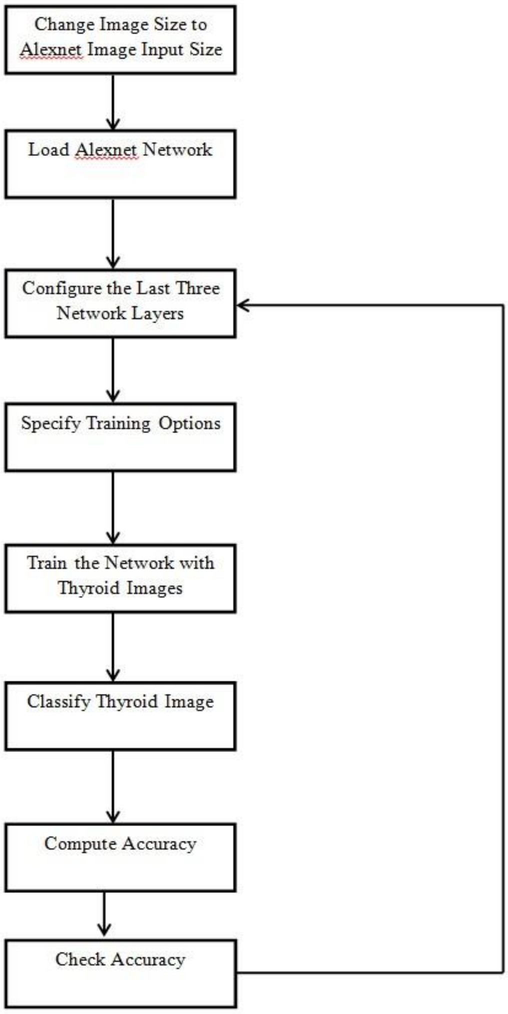

Figure 2 Flow Diagram for the Classification of Thyroid Nodules

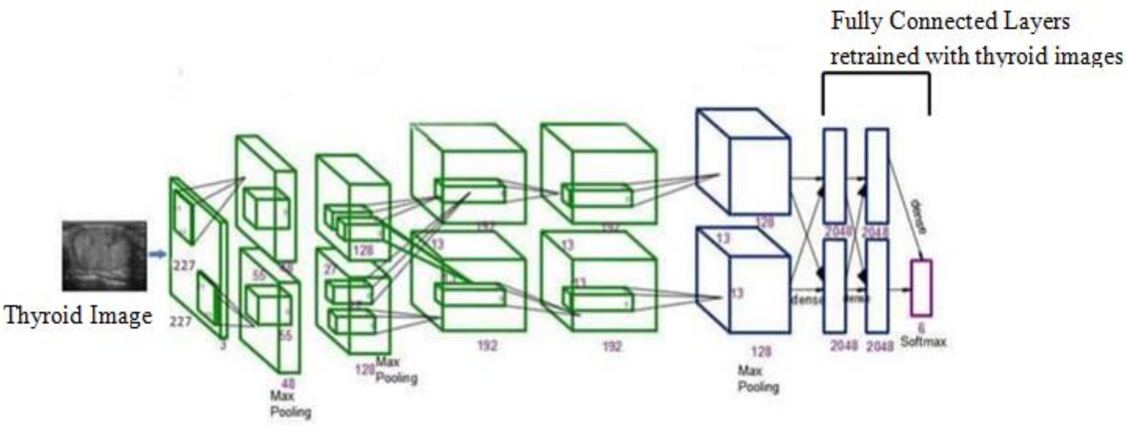

Figure 3 The Architecture of the Modified Alexnet Convolutional Neural Network.

3.4 Performance Evaluation of the Classification System

Accuracy, True Positive Rate (Sensitivity**)** and True Negative Rate (Specificity) in each category of thyroid nodules malignancy were determined in order to evaluate the performance of the classification system [20].Accuracy is the ratio of number of correct predictions to the total number of input thyroid images samples.

$$\text{Accuracy} = \frac{\text{True Positive} + \text{True Negative}}{\text{Total Number of Samples}}$$

Sensitivity is the proportion of positive data points that are correctly considered as positive, with respect to all positive data points.

$$\text{True Positive Rate} = \frac{\text{True Positive}}{\text{False Negative} + \text{True Positive}}$$

Specificity corresponds to the proportion of correct negative predictions divided by the total number of negatives

$$\text{True Negative Rate} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}}$$

In order to obtain the overall classification performance of the developed computer aided diagnosis system, the overall accuracy, average sensitivity and average specificity of the results were determined as follows [21] :

$$Overall\ accuracy = \frac{1}{N}\sum_{i=1}^{c} TP_i$$

$$Average\ Sesitivity = \frac{1}{N}\sum_{i=1}^{c} \frac{TP_i}{TP_i + FN_i}$$

$$Average\ Specificity = \frac{1}{N}\sum_{i=1}^{c} \frac{TNi}{TN_i + FP_i}$$

whereTPi, TFi, FNi, FNi, C and N are the true positives, true negatives, false positives, false negatives, total number of classes and number of instances respectively

III. Result and Discussion

The Confusion matrix for classification of thyroid nodules is as shown in Table 2. TP is the number of true positive predictions while FP is the number of false positive predictions for the considered class. TN and FN are the number of true negative predictions and false negative predictions respectively. All the tested thyroid nodules in TIRADS 2, TIRADS 3 and TIRADS 4a categories are correctly classified. In TIRADS 4b, 5 were correctly identified as TIRADS 4b while 1 was misclassified as 3, In TIRADS 4c, 7 were correctly identified as TIRADS 4c while 1 was misclassified as 4b. In TIRADS 5, 3 were correctly identified as TIRADS 5 while 1 was misclassified as 4c

Table 2: Confusion matrix for classification of Thyroid Nodules

		PREDICTED					
		TIRADS 2	**TIRADS 3**	**TIRADS 4a**	**TIRADS 4b**	**TIRADS 4c**	**TIRADS 5**
	TIRADS 2	9	0	0	0	0	0
	TIRADS 3	0	4	0	0	0	0
ACTUAL	**TIRADS 4a**	0	0	8	0	0	0
	TIRADS 4b	0	1	0	5	0	0
	TIRADS 4c	0	0	0	1	7	0
	TIRADS 5	0	0	0	0	1	3

The accuracy, sensitivity and specificity in each class is as shown in Table 3. Accuracy of TIRADS 2, TIRADS 3 and TIRADS 4a were 100%. This shows that all thyroid nodules in the three classes are correctly classified. Accuracy of TIRADS 4b, TIRADS 4c and TIRADS 5 obtained were 95%, 95% and 97%. This shows that abnormality can easily be identified with TIRADS 2, TIRADS 3 and TIRADS 4a at higher rate than TIRADS 2, TIRADS 3 and TIRADS 4a. It was observed that sensitivity of TIRADS 2, TIRADS 3 and TIRADS 4a were 100% while that of TIRADS 4b, TIRADS 4c and TIRADS 5 obtained were 83%, 88% and 75% respectively. This shows that the developed CAD system correctly identified the presence of abnormality in TIRADS 2, TIRADS 3 and TIRADS 4a at higher rate than TIRADS 4a and TIRADS 5.

Furthermore, the result in table 3 indicates that specificity of TIRADS 2, TIRADS 3 , TIRADS 4a and TIRADS 5 were 100% while both TIRADS 4b and TIRADS 4c were 97%. This shows that the presence of abnormality in TIRADS 2, TIRADS 3, TIRADS 4a and TIRADS 5 were correctly identified by the developed CAD system at higher rate than TIRADS 4b and TIRADS 4c.Ultrasound follow up is suggested for TIRADS 2 candidates. Biopsy candidates are those classified as category 4 or 5 (at least one suspicious feature). TIRADS 5 candidates are highly suggestive of malignancy.

The overall performance evaluation of the developed CAD system is as shown in Table 4. The developed CAD system achieved an overall accuracy of 92 %, average sensitivity of 91 % and average specificity of 99%. Most of the authors combined TIRADS 2 and TIRADS 3 as benign and TIRADS 4a, TIRADS 4b, TIRADS 4c and TIRADS 5a as malignant. Based on binary classification (benign and malignant), the developed classification system result in 100% accuracy, 100% sensitivity and 100 % specificity. The values of value of the accuracy, sensitivity and specificity obtained from the developed classification system based on six (6) class approach is less than that of binary based classification, which is in line with results obtained by Xiong, *et al.*,[22]. Xiong, *et al.*,[22] has shown that the performance of a classification system decreases with number of classes because multi-class classification increases data complexity.

Table .3: Performance Evaluation of the developed classification system

Classes	TP	FP	TN	FN	Accuracy (%)	Sensitivity (%)	Specificity (%)
TIRADS 2	9	0	30	0	100	100	100
TIRADS 3	4	0	35.	0	100.	100	100
TIRADS 4a	8	0	31.	0	100	100	100
TIRADS 4b	5	1	32	1	95	83	97
TIRADS 4c	7	1	30	1	95	88	97
TIRADS 5	3	0	35	1	97	75	100

Table 4.: Overall classification performance evaluation of the developed CAD system

Dataset	Overall Accuracy (%)	Average Sensitivity (%)	Average Specificity (%)
CIMLAB	92	91	99

IV. Conclusion

In this paper, a CAD system for classification of abnormalities in ultrasound thyroid nodules images was developed by a modified Alexnet and evaluated using accuracy, specificity and sensitivity. The CAD system is helpful for assessment of thyroid nodules and as a tool in follow-up diagnosis. The paper provides an effective method of classifying thyroid nodules into multiple stages of thyroid malignancies, which will be an aid to radiologists by providing second opinion for treatment procedures, follow up diagnosis and management procedures. Acquiring more thyroid images for training the pre-trained convolutional neural network could improve the performance of the diagnosis system. Computer aided diagnosis system for classification of abnormalities in thyroid nodules obtained from other imaging techniques such as computed tomography, X- Ray and Magnetic Resonance could also be developed using deep learning.

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