# Classification of focal liver disease in egyptian patients using ultrasound images and convolutional neural networks

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# ABSTRACT

Recently, computer-aided diagnostic systems for various diseases have received great attention. One of the latest technologies used is deep learning architectures for analyzing and classifying medical images. In this paper, a new system that uses deep learning to classify three focal diseases in the liver besides the normal liver is proposed. A pre-trained convolutional neural network is utilized. Two types of networks are used, ResNet50 and AlexNet with fully connected networks (FCNs). After extracting the deep features using deep learning, FCNs can input images in different states of the disease, such as Normal, Hem, HCC, and Cyst. Dataset is obtained from the Egyptian Liver Research Institute. Two classifiers are utilized, the first includes two classes (Normal/Cyst, Normal/Hem, Normal/HCC, HCC/Cyst, HCC/Hem, Cyst/Hem) and the second contains four classes (Normal/Cyst/ HCC/Hem) to distinguish liver images. Using performance criteria, it has been shown that the two-category classifiers have given better results than the four-class classifier, and accordingly a hybrid classifier was suggested to merge the weighted probabilities of the classes obtained by each singular classifier. Experimental results have achieved an accuracy of 96.1% using ResNet50 which means that it can be used as an assistive diagnostic method for classification of focal liver disease.

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#### 1. INTRODUCTION

One of the most vital organs in the human body is the liver, which is responsible for up to 500 different functions in combination with other organs and systems. Therefore, it is known that there is no natural or artificial organ that can be qualified for doing all functions of the liver. At the global level, the number of deaths as a result of liver disease is constantly increasing. Liver diseases are divided into two main types; the first type is focal diseases that affect a small area of the liver surface such as cyst, hematoma (Hem) and hepatocellular carcinoma (HCC). The second type of liver disease is the diffuse disease that affects the entire surface of the liver, such as fatty liver and cirrhosis [1].

It had been verified that the most important diagnostic tool for various diseases is medical images. In 1895, X-rays were discovered by Roentgen, whereby doctors were able to look inside the human body without surgery, and X-rays became the first method of diagnosis from that time. Since then, innovative types of imaging have been invented, such as ultrasound imaging (US), computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) [2].

Ultrasound (US) imaging is one of the most efficient methods for detecting clinical diseases. Ultrasound has many advantages such as safety, convenience, and low cost [3]. Despite these advantages, reading ultrasound is not at all easy. Therefore, some challenges are met when using ultrasound, such as heavy reliance on the operator's expertise or experience in diagnosis, as well as low imaging quality due to noise, artifacts, and other challenges [3]. Hence, it was found that when using ultrasound imaging, two major restrictions are faced; image quality and the personal experience of the physician. Therefore, it is necessary to develop methods for analyzing ultrasound images in a more objective, accurate and intelligent manner in order to help clinicians make the correct diagnosis.

Deep learning has played an important role in analyzing medical images [2]. It is a subfield of machine learbning which relies on deep neural networks (DNN). Recently, deep learning has gained attention due to its ability to extract features automatically from raw data. Moreover, it can process ultrasound images (object detection, organ segmentation, and classification) [2]. Convolutional neural network (CNN) is a type of neural networks which is particularly useful in image recognition and classification, and it has gained much attention from clinicians, academia, and industry [1].

Deep learning has the characteristic of nonlinear transformations. Through different algorithms, it can learn the input data using sundry processing layers with complex structures. It can also describe the input data in different ways. Images can be represented as vectors that contain pixel density values, a set of edges, and also regions of particular shape. Deep learning techniques can be categorized into three main categories; supervised deep networks, unsupervised deep networks, and hybrid deep networks [1]. Deep learning has replaced handcrafted feature extraction algorithms with unsupervised ones. Hence, there are many deep learning architectures models that can be applied to the analysis of ultrasound images such as CNNs, recurrent neural networks (RNNs), deep belief networks (DBNs), and autoencoders (AEs) [4].

Techniques that are based on deep learning have been adopted to diagnose different diseases. Liu et al. [5], presented a method for precocious diagnosis of both Alzheimer's disease (AD) and mild cognitive impairment (MCI) using auto-encoders and a softmax output layer, then they compared their method with support vector machines (SVM). Results had shown that, using auto-encoders outperformed the accuracy of SVM with accuracy of 87.76%. Wang et al. [6] presented a study to assess the condition of the liver (cirrhosis) and to determine what stage it is in, using deep learning through SWE images. They found that deep learning-based imaging is more accurate than 2-D SWE imaging to determine the extent of cirrhosis and advanced fibrosis, especially in patients with chronic liver disease B. Meng et al. [7], a finetuned VGGNet network and fully connected networks (FCNs) were utilized to predict liver status and fibrosis stage. Liu et al. [8] extracted liver features from ultrasound images using a pre-trained CNN model, then classified the liver condition as normal or abnormal using SVM. A deep-belief network model was trained by Wu et al. [9] to classify focal liver lesions based on time-intensity curves extracted from contrastenhanced ultrasound, and it had been shown that this method is superior to classical machine learning methods. Biswas et al. [10] used deep learning to assess fatty liver disease through ultrasound images. Hassan et al. [1] presented a proposal to extract the features from ultrasound images of the liver using a stacked sparse auto-encoder, then used the softmax layer to classify different focal liver diseases, and obtained a high classification accuracy compared to three other modern techniques. Pasyara et al. [11] proposed a deep classifier based on CNN to classify liver images. Several networks had been utilized; ResNeXt, ResNet18, ResNet34, ResNet50 and AlexNet which were followed by fully connected networks. A hybrid classifier which combines the weighted probabilities of the cases obtained by each individual classifier had been proposed. The results have showen an accuracy of 86%.

The present work aims to develop a framework for classifying focal liver disease based on US images using CNN in addition to a suggesting hybrid classifier to overcome the problems of overfitting, which may lead to extra costs during the training process. The diagnosis accuracy is a major consideration to help accurate diagnosis of focal liver disease.

The motivations of this study include defining a framework from two CNN models to optimize classification models for focal liver disease as well as proposing an accurate computer-aided design (CAD) system based on deep learning for image analysis, feature extraction, and classification. The main contributions of the present work can be summarized as follows:

- To study and compare different deep learning architectures for detecting focal liver disease
- To enhance the performance of deep learning training using data augmentation
- To increase the diagnosis accuracy using a suggested hybrid classifier

Deep learning techniques are utilized to classify the status of the liver (HCC, Cyst, Hem, or Normal liver) using ultrasound liver images. For this aim, two classifiers were trained to distinguish liver images, the first classifier is a two-class classifier (Normal/Cyst, Normal/HCC, Normal/Hem, Cyst/HCC, Cyst/Hem, and

Hem/HCC) and the second classifier is four-class classifier (Normal/Cyst/HCC/Hem). This classifier scores the probability of weights that each individual classifier has obtained. The rest of the paper is arranged as follows: section 2 gives the proposed system, section 3 introduces the research method, section 4 presents e xperimental results and discussions, and finally, conclusions are presented in section 5.

#### 2. PROPOSED SYSTEM

The present section represents a proposed system to diagnose four different liver conditions (Cyst, Hema, HCC, Healthy) using deep learning. Figure 1 shows a block diagram of the proposed system. The system consists of three main steps. In step 1, US images are segmented to extract the region of interest (RoI), and data augmentation is utilized to get better training capabilities of the proposed model through increasing the data volume. In step 2, transfer learning is applied by investigating two structures; ResNet50 [12] and AlexNet [13], to extract liver image features. In the final step, a softmax classifier is used to determine whether the disease is a Cyst, Hema, HCC, or a healthy liver.



Figure 1. The proposed system

#### 3. RESEARCH METHODS

As previously explained, the proposed system contains three basic modules. The first module is dedicated for the segmentation process. A data augmentation process is performed in the second module. In the last module, features are extracted. In the next subsections, each module will be presented in more detail.

#### **3.1. Image segmentation**

In general, image segmentation means partitioning an image into constituient parts to focus on essentials. In medical CAD systems, the region containing the disease is known as the RoI. In the present work, the RoI was was extracted using a level set method and a fuzzy C-means clustering algorithm. First, the contour of the liver lesions was initialized using a level set method. Then, it is extracted in an automatic way using the Fuzzy c-means clustering technique. Results of the segmentation step are shown in Figure 2.



#### 3.2. Data augmentation

Figure 2. RoI segmentation

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Data augmentation has been used to obtain more cases of ultrasound imaging, which prevents overfitting of the network and preserves the fine details of the training images. Moreover, it increases the robustness of the network against distortions in the image data [4]. In the proposed system, we made a flip from left to right as well as from top to bottom; vertical and horizontal translations were made with zero padding on each image. This has led to an augmented dataset with 1260 images instead of original dataset of 180 images.

#### 3.3. Deep feature extraction

Feature extraction step is one of the most sensitive steps in computer-aided design (CAD) systemsdue to the presence of a large number of variables and the huge size of datasets [14]-[19]. Feature extraction selects and aggregates variables into features. The amount of data being processed is effectively reduced without the lack of accuracy. Data reduction facilitates learning rates in the machine learning process. These features are used as inputs to the classification stage.

In the proposed system, a CNN has been used to extract image features. CNN architecture includes a convolutional layer, a pooling layer, rectified linear unit (ReLu), and, if needed, a batch normalization. When creating a standard multi-layer neural network, it is necessary to connect a network with fully connected layers in the last part of the network. In order to reduce the data rate of the layer, the subsequent pooling layer aggregates the output of the convolutional layer. In a standard CNN model, the distribution over classes is generally achieved through the softmax function in the last layer of network, by feeding activations. Sometimes, traditional machine learning methods can be utilized, such as majority voting [20] or linear SVM [8]. Due to its increasing prevalence and applicability in medical image analysis in particular, deep learning architectures based on CNNs have been progressing. Examples include AlexNet, GoogLeNet, ResNet, and VGGNet [4].

#### **3.3.1.** Transfer learning

A common method used in deep learning applications is transfer learning. When starting learning a new task, a pre-trained network must be used as a starting point. In cases of a small number of images, we resort to transfer learning. It includes many pre-trained image classification networks such as (AlexNet [12], VGGNet [21], ResNet [13], and ResNeXt [22]). These networks contain features that are convenient for a vast scope of images. The present work utilizes ImageNet database (ILSVRC) which includes more than one million images. The networks are trained using a subset of this database [23].

AlexNet [12] and ResNet [13] had been used in the proposed system as they achieved remarkable prosperity in the applications of medical engineering (detection of lung cancer [24], face recognition [25] and detection of breast cancer [26]-[29]). AlexNet architecture is shown in Figure 3. It consists of five convolutional layers, three pooling layers, and three fully connected layers [12], [30]. Each neuron in the convolution layers calculates the dot product between the weights and the local region connected to the input volume [31]. The pooling layer comes after every convolutional layer. This layer reduces the amount of computation and improves robustness by sampling down the spatial dimensions. The fully connected layers process them and output a vector that contains the most relevant features [31].



Figure 3. AlexNet architecture [12]

The architecture of ResNet-50 is shown in Figure 4. The main idea of residual network (ResNet) is the use of shortcut links to exceed block of convolutional layers [28]. This network leads to a perfect improvement in the capability and performance of the system [28]. Figure 5 illustrates the designed convolutional deep neural network (CDNN). The ultrasound images are fed into CDNN, then one value is

restorated for each ultrasound input image as output. During training, a fore and inversly pass are made through the net for each repetition. In forward pass, each layer performs its own activation function and applies it to the output of the preceding layer to produce the new outputs. Assuming that:

X1, ..., Xn : inputs from the previous layers.

Z1, ..., Zm : outputs.

L, the loss function calculated between the real goals and the foretelling.

T, the real goals.

Y, the predictions at the end of the fore pass.

In inversely pass, using the loss derivatives with consideration, the output of that layer calculates the loss derivative L for each layer with consideration its inputs and its weights. The chain rule is used to calculate the derivatives of the loss:

$$\frac{\partial L}{\partial X^{(i)}} = \sum_{j} \frac{\partial L}{\partial Z_{j}} \frac{\partial Z_{j}}{\partial X^{(i)}} \qquad i = 1, \dots, number of inputs and$$

$$j = 1, \dots, number of outputs \qquad (1)$$

$$\frac{\partial L}{\partial W_{i}} = \sum_{j} \frac{\partial L}{\partial Z_{j}} \frac{\partial Z_{j}}{\partial W_{i}} \qquad i = 1, \dots number of learnable parametes and$$

$$j = 1, \dots, number of outputs \qquad (2)$$



Figure 4. ResNet-50 architecture [32]

The initial weights were chosen by Gaussian distribution ( $\mu = 0, \sigma 2 = 1$ ). Bias is equal to 0 as initial value. Both weights and biases, which are known as network parameters, were updated and the loss function was reduced using Adam's algorithm [27]. The advantage of Adam's optimization algorithm is that it improves machine training. This algorithm uses learning rates which automatically adapt to the loss function that is being optimized. In other algorithms, as the gradient descent algorithm, for all parameters only one learning rate can be used. An element-wise moving average strategy and an added momentum term were used:

$$m_{l} = \beta_{1} m_{l-1} + (1 - \beta_{1}) \nabla E(\theta_{l})$$
(3)

$$v_2 = \beta_2 v_{l-1} + (1 - \beta_2) [\nabla E(\theta_l)]^2$$
(4)

where:

1, iteration number,

 $\theta$ , parameter vector,

 $E(\theta)$ , loss function,

 $\beta_1$  and  $\beta_2$ , decay rates.

Adam's algorithm updates the network parameters by using the moving averages as (5).

$$\theta_{l+1} = \theta_l - \frac{\alpha m_l}{\sqrt{\nu_l + \varepsilon}} \tag{5}$$

Where  $\alpha > 0$  is the learning rate and  $\varepsilon$  is a small constant added to avoid division by zero.

)



Figure 5. The architecture of designed convolutional deep neural network

The activation function rectified linear unit (ReLU) layer has been used in deep convolutional neural networks. A threshold operation is performed on each of the input elements, so that any value less than zero is set as zero. By using mini-batch, the input of each layer was normalized. Speeding up training with lower sensitivity to network initialization has been achieverd using a batch normalization layer. The learning rate was selected to be  $10^{-4}$ . In order to reduce the training overfitting, two steps were applied; firstly, in the pre-trained models, the weights of the convolutional layers are transferred without training, secondly, only the fully connected layers are trained. Transfer learning can be applied to the CNN models by replacing the last fully connected layer of the pre-trained models (FC8 layer in AlexNet or FC1000 layer in ResNet50) with the fully connected designed networks (FCNs) shown in Figure 6. A three-layer convolutional network with 3×3 filters was used and images passes for it as input. Three fully connected layers were used to process data.



Figure 6. Architecture of the designed fully connected network

#### 3.4. Classification

Based on deep learning, focal liver disease was diagnosed by adding a softmax layer to represent the input data class label. If it is desired to determine the number of units in the softmax layer, it must be equal to the number of classes. For the network output, it is interpreted as the class membership probabilities (p (y=j|x), where j=1,...,k). Because of each output unit is specific to a particular class, the activation function must meet the following limitaions:

$$0 \le \sigma(x)_i \le 1 \text{ and } \sum_{k=1}^k \sigma(x)_i = 1, \tag{6}$$

where  $\sigma(x)_i$  is defined as the output of the output unit i. The softmax activation function is [26]:

$$p(y = c_i | x) = \sigma_i = \frac{e^{z_i}}{\sum_{j=1}^k e^{z_j}}$$
(7)

where  $z_i$  is the total weighted sum of inputs to the output unit i, and k denotes the number of classes.

#### 3.4.1. The hybrid classifier

When limitations arise, for instance when certain data are rare or difficult to obtain such as medical images, or when computing power is scarce, such as in embedded applications, a possible solution is to combine different classification models. This is the main concept of hybrid classification which seeks to exploit strengths of the individual works and to obtain enhanced performance by merging them [33], [34].

In the present study, seven classifiers were trained to classify liver images into four different classes; Normal, Cyst, Hem, and HCC. The first six classes were used to distinguish between Normal/Cyst, Normal/Hem, Normal/HCC, HCC/Cyst, HCC/Hem, Cyst/Hem. The last classifier was used to classify the ultrasound images of the liver into four categories of liver diseases, namely Normal/Cyst/ HCC/Hem. Based on results, it was found that two-class classifiers work more efficiently than four-class classifiers. So, a hybrid classifier has been proposed to address this issue. It consists of all the trained classifiers and aggregates their outcoms using the weighted probabilities of the classes obtained by each singular classifier. In each classifier the probabilities of all classes for each input data were defined by using a softmax output layer. To define a final label to the sample, these weighted probabilities were used. Also, to define the proper weights for the outputs of each classifier, a net search was used. The weights vary from 0 to 1 with a step size of 0.125. Based on the performance of classification, the best composition was selected. Finally, in order to normalize the weights, each ideal weight was divided by the overall sum of weights. The block diagram of hybrid classifier is shown in Figure 7. The figure demonstrates six classifiers to diagnose among two different diseases. For example, the first classifier differentiates between Normal and HCC, the second one between Noraml and Hem and so on. The 7th classifier diagnoses among Normal, Cyst, Hem, and HCC. Finally, the obtained probabilities from the classifiers of the same disease are added to obtain the final probability of that disease. For example, the probabilities for HCC disease obtained from the first, forth, fifth, and seventh classifiers are added to obtain the final prbability of diagnosis HCC disease. The rest of diseases are obtained in the same manner.



Figure 7. Block diagram of hybrid classifier

#### 4. EXPERIMENTAL RESULTS

### 4.1. Dataset and data acquisition

A set of ultrasound image data was collected from the Egyptian Liver Research Institute and the Sherbin Central Hospital, Dakahlia Governorate, Egypt. Each image contains one of the focal liver lesions, including Cyst, Hem, or HCC. A total of 180 liver ultrasound images (30 Normal, 70 Cyst, 40 Hem, and 40 HCC) ranging in age from 29 to 80 years. This dataset had been augmented to get a total size of 1260 images.

Before submitting the images to the network, liver regions were cropped from the ultrasound images. Images are then resized to maintain the resolution and aspect ratio in the sidy and pivotal directions. A square window is taken out from the liver area, the area of interest is chosen, including the part containing the disease to be detected, or the largest part of the liver tissue in the case of a healthy liver. Accuracy, sensitivity, and specificity were used as performance measures to evaluate diagnostic results [35].

- Accuracy is defined as the percentage of correct classifications and is calculated as (8).

$$Accuracy = \frac{TP+TN}{TP+FP+TN+FN} \times 100$$
(8)

– Sensitivity is defined as the true positivity rate and is calculated as (9).

$$Sensitivity = \frac{TP}{TP+FN} \times 100$$
(9)

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- Specificity is known as the real rate of negativity and is calculated as (10).

$$Specificity = \frac{TN}{TN+FP} \times 100$$
(10)

In order to evaluate the performance of classification for the results of four types of liver states, data were randomly divided into training (70%) and validation (30%) sets. When classifying the liver images into four categories, it has been found that, training the proposed CDNN had led to a lower accuracy than using the pre-trained networks. The diagnosis performance when using the most well-known pre-trained networks, namely ResNet50 and AlexNet for two-class classifiers is shown in Table 1. It has been verified that the ResNet50 network has better accuracy than AlexNet network for each of the two-class classifiers.

Table 2 shows the accuracy of classification when using the hybrid classifier in the proposed system compared with the accuracy when using the four class classifier. It has been shown that the accuracy of the proposed system when using ResNet50 and AlexNet outperforms the accuracy of using four class classifier. Also, the accuracy when using the ResNet50 networks give better performance than the accuracy obtained when using the AlexNet network.

Network	Groups	Accuracy	Senstivity	Specificty
AlexNet	Normal/HCC	92.3%	96.1%	87.7%
	Normal/Hem	91.6%	94.6%	85.4%
	Normal/Cyst	92.1%	94.9%	83.5%
	HCC/Hem	93.7%	97.5%	76.9%
	HCC/Cyst	93.8%	96.7%	80.8%
	Hem/cyst	91.9%	96.8%	82.1%
ResNet50	Normal/HCC	95.2%	97.2%	89.1%
	Normal/Hem	93.6%	95.4%	86.4%
	Normal/Cyst	95.2%	96.6%	83.8%
	HCC/Hem	94.8%	95.9%	84.6%
	HCC/Cyst	94.9%	94.7%	88.3%
	Hem/cyst	93.6%	96.2%	87.1%

Table 1. Results of diagnostic system for distinction between two classes

Table 2. Classification performance of networks when using proposed system and without using it

Network	Accuracy of 4-Class Classifier	Accuracy (Proposed system)
AlexNet	80.6%	89.8%
ResNet50	87.7%	96.1%

# 4.2. Discussion

Through experiments using the deep neural network model, the following remarks had been observed. First, liver images were classified into normal, Hem, Cyst and HCC. Second, the effectiveness of using deep features had been proven due to the rich information they contain. Third, when the sample size becomes smaller, it is not appropriate to train a CDNN from the beginning, so pre-trained networks are used as a starting point. Actually, the results were enhanced dramatically when the final fully connected layers were retrained.

According to the reslts in Tables 1 and 2, it was noticed that, in the case of classifying liver images into two categories, the performance of the networks was relatively high, while the level of accuracy was less than the required level in the case of classification into four categories. According to the results obtained, we have a better classification performance of the two categories and the accuracy was 95.2%, while in the case of classifiers by amalgamating the likely probability of predictions obtained by each singular classifier, and from the results, we found that the final accuracy had been improved, as we obtained an accuracy of 96.1% in distinguishing the four classes of liver images. The main limitation of the present study is the limited number of cases. In the future, it is intended to improve results using a larger dataset.

### 5. CONCLUSION

On the small medical datasets, to build an effective classifier, we can use fine-tuning for an already present deep convolutional neural network like ResNet50 and AlexNet. In this paper, a new framework is proposed for classification of three focal liver diseases, Hem, Cyst and HCC, in addition to normal liver.

A two-class (normal/ Hem, normal/HCC, Normal/Cyst, Hem/HCC, Hem/Cyst, HCC/Cyst) and a four-class (Normal/Cyst/HCC/Hem) classifier were trained to classify these liver ultrasound images. Results had shown that the two-class classifiers had given a better performance when compared with the results obtained from the four-class classifier. Therefore, a hybrid classifier was proposed in which we combined the weighted probabilities of the classes obtained from each singular classifier. The accuracy had reached 96.1% which confirmed that the proposed technique can serve as an effective diagnostic tool for liver diseases. In future, it will be benifitial to use a large data set along with more fine-tuning of the CNN to get better performance and strength of results.

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