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Classification of Focal Liver Diseases Using Pre-Trained Convolutional Neural Networks

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Abstract

Recently, there has been a great interest in computer aided diagnostic systems for various diseases. One of the latest technologies used is deep learning architectures for analyzing and classifying medical images. In this paper, a system is proposed that uses deep learning to diagnose three focal diseases in the liver besides the normal liver. In our proposed system, we used a pre-trained convolutional neural network. Two types of networks were used, namely ResNet50 and AlexNet with fully connected networks (FCNs). After extracting the deep features using deep learning transfer, we will have enough classification information. Then, FCNs can puts images in different states of the disease. such as normal, Hem, HCC, and Cyst. Two classifiers are also trained, the first classifier consists of two classes (Normal/Cyst, Normal/Hem, Normal/HCC, HCC/Cyst, HCC/Hem, Cyst/Hem) and the second classifier consists of four classes (Normal/Cyst/ HCC/Hem) to distinguish liver images. Experimental results showed an accuracy of 95.2% using ResNet50.

1. Introduction

The liver is one of the most vital organs in the human body. It is thought to be responsible for up to 500 separate functions, usually in combination with other organs and systems. At the moment, no artificial organ or organ is capable of performing all the functions of the liver. Therefore, without a healthy liver, we cannot be alive. At the global level, the number of deaths as a result of liver disease is constantly increasing. There are two main types of liver disease, focal and diffuse disease. Focal diseases affect a small area of the liver surface, such as cyst, hematoma (Hem), and hepatocellular carcinoma (HCC) while diffuse diseases affect the entire surface of the liver, such as fatty liver and cirrhosis [1].

One of the most important diagnostic tools 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, imaging methods have varied, and innovative types of imaging have been invented, such as ultrasound imaging, magnetic resonance imaging, and positron emission to mography. [2]

Ultrasound (US) imaging is one of the most used methods for detecting clinical diseases. Ultrasound has many advantages such as safety, convenience and low cost. Despite these advantages, reading ultrasound is not at all easy. Therefore, we face some challenges 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. Hence, we find that when we rely on ultrasound imaging, we are subject to two main limitations: (1) image quality. (2) The personal experience of the physician. Usually, the doctor evaluates the ultrasound images by visual examination, but the characteristics that can be determined by the human eye are limited. In addition, the same ultrasound image can be interpreted differently by doctors with different clinical experience. Therefore, we found it 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.

Although many machine learning approaches have been introduced to diagnose many liver diseases, in most of these methods shallow data are used (multi-layer neural network (MLP) and support vector machines (SVM) are examples of shallow data). However, it has been proven that Artificial Neural Networks (ANNs) and SVM devices provide good accuracy in diagnosis and are also effective when used in CAD systems. These types of architectures contain a single layer of nonlinear feature transformations and do not have multiple layers of condensing nonlinear features. [1]

In recent years, deep learning has played an increasingly important role in medical image analysis. Deep learning is at the forefront of artificial intelligence and a subfield of machine learning and is based on deep neural networks DNN (neural networks that contain more than one hidden layer). Deep learning has gained much attention for being able to automatically extract features from raw data and

holds the potential to process ultrasound images involving several tasks, such as classification, object detection, and organ segmentation. A type of neural network is particularly useful in image recognition and classification, it is considered a subcategory of DNN and have been attracting a lot of interest from industry, academia, and clinicians, namely, convolutional neural networks (CNN).[1]

This study aims at investigating whether liver status (normal, Cyst, Hem, or HCC liver) could be classified based on dynamic ultrasound images using deep learning techniques. For this purpose, two- class (normal/Cyst, normal/HCC, normal/Hem, Cyst/HCC, Cyst/Hem, and Hem/HCC) and three-class (Normal/Cyst/HCC/Hem) classifiers were trained for distinguishing liver images. Then a hybrid classifier is proposed that aggregates the weighted probabilities of the classes obtained by each classifier and selects the class using a majority voting strategy. The paper is organized as follows: In section 2, background study of deep learning. In section 3, we introduce the data and the study procedure adopted for data processing and classification. In section 4, we present the obtained results. Section 5 provides some discussions about the results, and finally, conclusions are drawn in section 6.

2. Background survey and important feature of this research

Deep learning is the latest method of machine learning in many applications. There are many techniques used to diagnose different diseases based on deep learning. In this paper, we will review techniques used in diagnosing diseases based on features extracted from medical images using deep learning. For example, Liu et al. [3], presented a method for early diagnosis of both Alzheimer's disease (AD) and Mild Cognitive Impairment(MCI) using a stacked auto-encoders and a softmax output layer, then compared this method with SVM. The results showed that, using auto-encoders outperformed the accuracy of SVM with accuracy of 87.76%. whereas the accuracy of SK-SVM and MK-SVM were 84.4% and 86.42%, respectively.

Wang et al [4] presented a study to assess the condition of the liver (cirrhosis) and 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.

In Meng et al [5], A fine-tuned VGGNet network and FCN were used to predict liver status and fibrosis stage. Also, Liu et al [6] 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 [7] to classify focal liver lesions based on time-intensity curves extracted from contrast-enhanced ultrasound, and they showed that this method is superior to classical machine learning methods.

Biswas et al [8] used deep learning to assess fatty liver disease through ultrasound images and performed well and better than machine learning approaches. Tarek 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.

Pezhman Pasyara,b, et al.[9] proposed a deep classifier consisting of convolutional neural networks, in which several networks were used: ResNeXt, ResNet18, ResNet34, ResNet50 and AlexNet which concatenated with fully connected networks, the extracted deep features were obtained using transfer learning and thus put the images into different states of the disease. It turned out that the two-class classifiers showed better performance, so a hybrid classifier was proposed to integrate the weighted probabilities of the classes obtained by each individual classifier. The results showed an accuracy of 86% using a hybrid classifier for liver images.

3. Proposed system

This section represents the proposed system that uses deep learning to diagnose three focal liver diseases along with the normal liver. Figure 1 represents our proposed In system, which consists of three main steps. In step 1, data

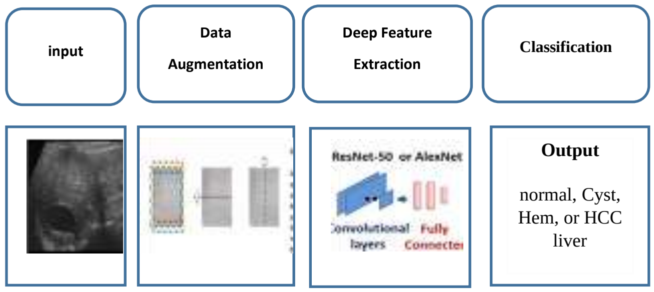

Figure 1: proposed system

augmentation is used to increase the data in order to improve the training capabilities of the proposed deep learning model. step 2, a transfer learning is applied by investigating two structures (ResNet50 [13] and AlexNet[14]) to extract liver image features. Finally, a softmax classifier is used to classify the focal liver diseases to be a Cyst, Hem, HCC, or a healthy one. These steps are presented in detail in the sequent subsections.

Step1: Data augmentation

In addition, 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, as well as increases the robustness of the network against distortions in the image data [10]. For example, we can add random rotations to the training input to make the trained network invariant to the rotations of input images. We applied (1) 2-pixel horizontal and vertical translations with zero padding, and (2) left-right and up-down flippings to every pre-processed image. This adds 1080 further images (augmented images) to the original dataset (consisting of 180 images).

Step 2: Deep feature extraction

Feature extraction is a process of dimensionality reduction by which an initial set of raw data is reduced to more manageable groups for processing. A characteristic of these large data sets is a large number of variables that require a lot of computing resources to process. Feature extraction is the name for methods that select and /or combine variables into features, effectively reducing the amount of data that must be processed, while still accurately and completely describing the original data set.

The process of feature extraction is useful when you need to reduce the number of resources needed for processing without losing important or relevant information. Feature extraction can also reduce the amount of redundant data for a given analysis. Also, the reduction of the data and the machine's efforts in building variable combinations (features) facilitate the speed of learning and generalization steps in the machine learning process.

Features extraction is one of the sensitive step in CAD systems [15, 16, 17, 18, 19, and 20. These features are used as inputs to a classifier. Since most of the liver US images consist of irregular and diffused regions.

a. Deep Neural Network Architecture

Deep learning is a machine learning technique that contains many nonlinear transformations. by using different algorithms, it can learn the representation of input data using several processing layers with complicated structures. It can also describe the input data in different ways, for example images can be represented as vectors of pixel intensity values, a variety of edges, and regions of a particular shape. We also see that; deep learning has replaced handcrafted feature extraction algorithms with unsupervised ones. Hence, there are many deep learning architectures such as convolutional neural networks, autoencoders, deep belief networks, and recurrent neural networks [1]. Since in our proposed system, we have used the Convolutional Neural Network architecture, it is discussed in the below section.

Deep learning architectures can be categorized based on deep learning architectures and techniques into three main categories: supervised deep networks or deep discriminative models, unsupervised deep networks or deep generative models, and hybrid deep networks. The basic models that are applied in the analysis of current ultrasound images are mainly CNNs, recurrent neural networks (RNNs), RBMs/DBNs (where DBN refers to deep belief networks), AEs, and variants of these deep learning architectures [10] Since in our proposed system, we have used the Convolutional Neural Network architecture, it is discussed in the below section.

b. Convolutional Neural Networks

CNNs are a type of deep discriminative architecture that includes several modules, each module consisting of a convolutional layer and a pooling layer. These are followed by other layers ،such as a rectified linear unit (ReLu), and if necessary batch normalization. To form a standard multi-layer neural network, the last part of the network is connected with fully connected layers. To reduce the data rate of the layer below, the output of the convolutional layer is aggregated by the subsequent pooling layer. Together with the chosen pooling schemes, the weight shared in the convolutional layer can imbue certain invariant properties to the CNN, such as translational invariance. This can also greatly reduce the number of parameters; for example, the number of weights no longer absolutely depends on the size of the input images. Note that fully connected layers, usually no longer share the weights. In a standard CNN model, Through the softmax function in the last layer of network, the distribution over classes is generally achieved by feeding activations, however, several conventional machine learning methods are used alternatively ، such as voting strategy [11] or linear SVM [12]. Given their increasing popularity and practicability, many classical and CNN-based deep learning architectures have been developed and applied in (medical) image analysis, NLP, and speech recognition. Examples include AlexNet (or CaffeNet, which is suitable for the Caffe deep learning framework), LeNet, faster R-CNN, GoogLeNet, ResNet, and VGGNet.[10]

our designed convolutional deep neural network (CDNN) is illustrated schematically in Fig. 3. In summary, the final modified ultrasound images are fed into the CDNN, and the samples are taken down by dividing the input into rectangular regions and calculating the maximum value for each region by the maximum pooling layer. This reduces the number of parameters that must be learned and thus prevents over-fitting. Then one value is returned for each ultrasound input image as output. During training, for each repetition a forward and backward pass is made over the net. In the forward pass, each layer performs its own activation function on the output of the previous layer to generate the new outputs. Assuming X1, …, Xn are inputs from the previous layers and outputs Z1, …, Zm for the next layers, then the loss function L is calculated between the real goals T and the predictions Y at the end of the forward pass. While during back-pass, each layer calculates the loss derivative L with respect to its inputs and its weights using the loss derivatives with respect to the output of that layer. To calculate the derivatives of the loss, the chain rule can be used:

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

$$j = 1, \ldots \ldots, number\ of\ outputs$$

$$\frac{\partial L}{\partial W_i} = \sum_j \frac{\partial L}{\partial Z_J} \frac{\partial Z_J}{\partial W_i} \qquad i = 1, \ldots \ldots number\ of\ learnable\ parametes\ and$$

$$j = 1, \ldots \ldots \ldots \ldots \ldots, number\ of\ outputs$$

The initial weights have a Gaussian distribution with a mean of 0, and a standard deviation of 0.01 (N(μ =0,σ2 =1)). The initial bias value is 0.

We updated the network parameters (weights and biases) and reduced the loss function by using Adam's algorithm [21]. Gradient descent algorithm uses one learning rate for all parameters. Whereas, Adam's optimization algorithms use learning rates that automatically adapt to the loss function being optimized and thus improve network training. It uses an added momentum term and an element-wise moving average strategy:

$$m_l = \beta_1 m_{l-1} + (1 - \beta_1)\nabla E(\theta_l)$$

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

Where l is the iteration number, θ is the parameter vector, $E(\theta)$ is the loss function, β_1 and β_2 are the decay rates. Adams uses the moving averages to update the network parameters as:

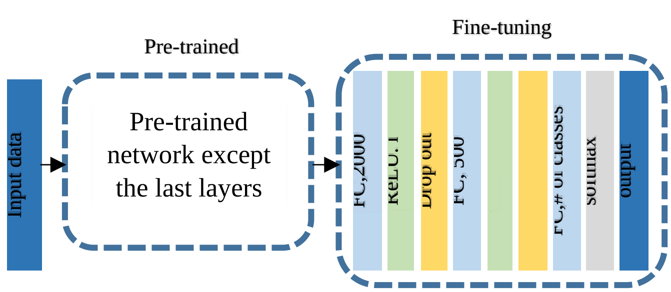

Figure 2: the architecture of our designed CDNN

$$\theta_{l+1} = \theta_l - \frac{\propto m_l}{\sqrt{v_l} + \varepsilon}$$

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

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. The input of each layer is also normalized across a mini-batch, and speeding up training while reducing sensitivity to network initialization by using a batch normalization layer. 0.0001 was selected for learning rate through trial and error.

The input images were passed through a network with three convolutional layers with 3 × 3 filters. The data were then processed with three fully connected layers having 2000, 500, and 7 (number of classes) hidden neurons, respectively.

c. Transfer learning

Transfer learning is commonly used in deep learning applications. A pre-trained network is used as a starting point for learning a new task, as training a network from scratch using random starting weights results in a network that is much slower and more difficult, unlike fine-tuning the network using transfer learning, especially in cases that contain a small number of images. Pre-trained image classification networks (such as AlexNet [13], VGGNet [22], ResNet [14], and ResNeXt [23]) contain learned rich features suitable for a wide range of images. These networks are trained on a subset of the ImageNet database (ILSVRC) [24], which contains more than a million images falling within 1000 object classes. We used one of these networks to transfer learning.

Step 3: Classification

The last layers of this pre-trained network are configured for 1000 classes. Therefore ،important to reconfigure and adjust it for the intended classification task. We have replaced the last layers of this network with the fully connected designed networks (FCNs) shown in Figure 3.

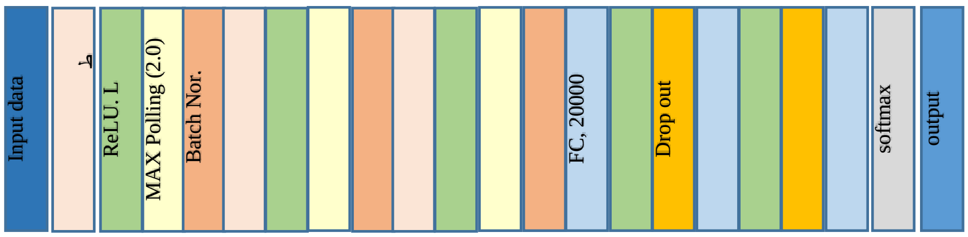

Figure 2: the architecture of our designed fully connected network, concatenated to pre-trained network.

4. Experimental results

Dataset, Data acquisition and adjustment for training

There is still no standard database of images that will be used to diagnose liver disease. So the photos are assembled by individual efforts. Here, a set of ultrasound image data was collected from the Egyptian Liver Research Institute and the Sherbin Central Hospital, Dakahlia Governorate. Each image contains one of the focal liver lesions, including a Cyst, Hem, or hepatocellular carcinoma HCC. A total of 180 liver ultrasound images were collected, ranging in age from 29 to 80 years.

Liver regions are manually cropped from the original images and resized by an experienced radiologist to maintain resolution and aspect ratio in the lateral and axial directions. Before submitting the images to the network, a square window is extracted from the liver area, and 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.

Based on the use of deep learning and dynamic ultrasound images, this section presents the classification performance evaluation results of four types of liver status, namely Normal/Cyst/ HCC/Hem liver. This study included 180 ultrasound examinations (30 Normal liver ultrasound images, 70 Cyst images, 40 Hem images and 40 HCC images) each assigned to one of the four classes based on biopsy specimens. We randomly divided the data into training (70%) and validation (30%) sets. When we train networks for deep learning, it is often useful to monitor the training progress.

In classifying liver images into four categories, we find that training the proposed CDNN from scratch leads to an accuracy of 61%. While the diagnostic performance of some well-known networks, such as ResNet50 and AlexNet for the four-class classification are shown in Table 1, that shows the relevant diagnostic results of the two-class classifiers using the above networks. “Sensitivity”, “Specificity”, and “Accuracy” were used to evaluate diagnostic results ‹which are defined as follows:

$$\text{Accuracy} = \frac{TP+TN}{TP+FP+TN+FN} \times 100$$

$$\text{Sensitivity} = \frac{TP}{TP+FN} \times 100$$

$$\text{Specificity} = \frac{TN}{TN+FP} \times 100$$

5. Discussion

Through our experiments using the deep neural network model, we found the following: First: Liver images (ultrasound) were classified into normal, Hem, Cyst and HCC. Second: The effectiveness of using deep features has been proven due to the rich information they contain. Third: Training the CDNN from scratch is not feasible due to the small sample size. So pre-trained networks are used as a starting point. in fact ‹When the final fully connected layers are retrained, this adapts the classification stage to the task at hand and enhances the results significantly.

Looking at Table 1, we find that the examined networks had a relatively high performance in classifying liver images into two categories. While the classification into four categories did not lead to the required level of accuracy.

According to the results obtained, ResNet50 has a better performance in the classification of the two categories and the accuracy was 95.2% with a sensitivity of 97.2%, while in the case of classification of four categories the accuracy was 79%. The main limitation of this study is the small sample size. In the future, we can get more accurate results when accessing a large data set.

Table 1: Diagnostic results for distinction between two class (Normal/ Hem, Normal/HCC, Normal/Cyst, Hem/HCC, Hem/Cyst, HCC/Cyst)

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%

6. Conclusion

Fine-tuning an existing deep convolutional neural network such as ResNet50 and AlexNet can be used to construct effective classifiers on the small medical datasets. In this study, a new framework is proposed for classification of Normal, Hem, Cyst and HCC liver images based on a hybrid classifier. Two-class (normal/ Hem, normal/HCC, Normal/Cyst, Hem/HCC, Hem/Cyst, HCC/Cyst) and four-class (Normal/Cyst/HCC/Hem) classifiers were trained to distinguish these liver images. Since two-class classifiers showed better performance compared to the four-class classifiers. Further tuning of the CNN along with using a larger dataset is necessary to improve the performance and robustness of the results.

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