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Advances in Deep Learning Techniques for the Detection of Cancer: A Review

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***Abstract*—Deep learning is contributing the high level of services to the healthcare sector. As the digital medical data is increasing exponentially with time, early detection and prediction of diseases is becoming more efficient because of the deep learning techniques which reduce the fatality rate to a great extent. The main focus of this paper is to provide the comprehensive review about deep learning in the domain of medical image processing and analysis. We have demonstrated the use of new deep learning architectures in oncology for the prediction of different types of cancer like brain, lung, skin, etc. The state-of-the-art architectures effectively carry out analysis of 2D and 3D medical images to make the diagnosis of patient faster and more accurate. The use of popular approaches of machine learning such as ensemble and transfer learning with fine-tuning of parameters improve the performance of the deep neural networks in medical image analysis. The existing deep networks urge the new image classification network called Capsule Network (CapsNet) to make the classification and detection comparatively better. The equivariance characteristics of CapsNet makes it more influential as it discourages the effect of any structural invariance of an input image on the network.**

***Keywords*—cancer, convolutional neural network, 3D CNN, capsule network, transfer learning, ensemble learning, deep learning**

I. Introduction

The automated imitation of the brain is an emerging technology and has driven large focus and attention of the researchers and big research organizations towards itself. Deep Learning is the subfield of machine learning which uses techniques inspired by learning ability of the human brain. The deep neural network is the neural network with many layers and the architecture of these deep nets is a little complicated but is computationally stronger than any other machine learning methods like Linear Regression, Logistic Regression, k-nearest neighbors, Support Vector Machine (SVM), Random forest, etc. Deep neural networks have the hierarchical architecture where each layer categorizes some information, makes modifications and finally passes this information to the next layer. These networks are trained on many levels of concepts, ideas and abstractions ranging from simple to complex ones. Deep learning has set its flag in many fields like Natural Language Processing, Computer Vision, Prediction analysis, etc. It has emerged as the powerful tool and produces phenomenal results in many applications like image processing, object detection, text summarization, machine translation, game playing etc. Many companies like Google's Deep Mind, Apple, IBM, Microsoft, NVIDIA, etc. are using the deep learning techniques for building up new technologies. Horus Technology with its fascinating innovation helps the blind people to see. They are developing a wearable device that uses computer vision, deep learning, and GPUs to understand the surrounding environment and describe it to users [1] so that they get the insight of the things around them. Along with other applications, deep learning is deployed at the front lines of healthcare and has produced the influential results by analyzing huge electronic medical data for the treatment of the diseases. Researchers showed that they could predict heart failure nine months before the traditional techniques [1]. The future of personalized medicine is expected to be accomplished by deep learning techniques. The researchers in Imperial College London are working to automatically provide the assessment of brain damage very fast [38]. Enlitic, the San Francisco-based startup is using deep learning to build solutions and the state-of-the-art clinical decision support products [39]. Arterys is the AI assistance to the radiologist and provides to quantify and visualize the heart flow in the body using MRI machine [1], [40]. Researchers in University of Toronto are working on the cancer-causing mutations using deep learning [41]. Deep Genomics are using deep learning to understand the variations of the genes that cause diseases [1].

Deep learning techniques are used for analyzing X-Rays, CT Scans and MRIs images which has improved detection, diagnosis, and treatment of disease. Cancer is a deadly disease and the number of patients suffering from cancer is increasing rapidly. Indian Council of Medical Research (ICMR) stated in 2016 that the total number of new cancer cases is expected to reach nearly 17.3 lakh in 2020 [2]. The early detection of such deadly disease can reduce the fatality rate and the deep learning methods have proved to be beneficial in the early detection of diseases. The deep nets in medical diagnosis are more efficient than the previous image processing techniques. One of the state-of-the-art architecture used in deep learning image processing is Convolution Neural Network (CNN or ConvNet). The CNN is very effective in the areas of image recognition and classification problems. This technique of deep learning has provided remarkable results in many competitions

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TABLE I
STATE-OF-THE-ART ARCHITECTURES INTRODUCED IN IMAGENET LSVRC

Architecture	Layer	Improvement	Top-5 error (Classification)	Training time	GPU	Parameters	Winner
AlexNet	8	ReLU was used first time	16.4	6 days	2	60 Million	2012
VGG	19	Replaced filters used in AlexNet with multiple 3x3 filters	7.3	2-3 weeks	4	138 Million	2014
GoogLeNet	22	Inception module and avg. pooling	6.7	2 weeks	8	25 Million	2014
ResNet	152	Residual modules	3.5	2-3 weeks	8	60 Million	2015

like ILSVRC for classification of images, PROMISE12 for prostate segmentation, BARTS 2013 for detection of brain tumor, LUNA16, KAGGLE DATA SCIENCE BOWL 2017 for detection of lung cancer.

Yann LeCun et al. [3] proposed the hierarchical architecture network of CNN called LeNet5 for recognition of characters. The main building blocks of ConvNets are Convolution, Squashing Function (Rectified Linear Unit), Pooling or Sub Sampling and Classification (Fully Connected Layers) as shown in Fig. 1. CNN automatically detects the unique features of the image that classifies it into its respective class.

Different popular architectures of CNN introduced after LeNet5 are AlexNet (8 layers), VGG (19 layers), GoogLeNet (22 layers), ResNet (152 layers) and emerged as ILSVRC winners at their respective years of introduction. This shows that different architectures or making the networks deep has helped in achieving higher accuracy. CNN requires a large amount of data to train and lacks to detect any kind of structural changes in an image. So, another model called CapsNet [37] helped to resolve this issue by understanding the change in rotation or proportion and adapt itself accordingly so that the spatial relationship inside an image is not lost. The CapsNet does not need so much data to train and so is the relief when stuck with limited data. It is the nested set of neural layers in a single layer which preserves equivariance and its contribution in to medical science will be a captivating research.

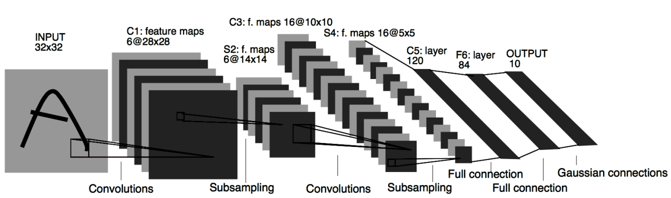

Fig. 1. Architecture of LeNet by Yann LeCun et al. [3] in 1998

II. RELATED REVIEW

A. Computer-Aided analysis for medical images

The four principle stages of medical image analysis are image capture, image enhancement, image segmentation and feature extraction. Medical images such as X-Rays, CT Scans, MRIs, etc are captured for analysis and diagnosis of disease. M. S. Al-Tarawneh [4] have mentioned image enhancement methods such as Gabor Filter, auto enhancement algorithm and Fast Fourier Transform (FFT) to improve the quality of the image. To get the region of interest the author has used Threshold approach and Marker-Controlled Watershed Segmentation and for feature extraction, Binarisation and Masking approaches are used. Similarly, there are many other methods that can be used for enhancement, segmentation and feature extraction such as Histogram equalization, Adaptive Histogram Equalization, CLAHE, Histogram of oriented gradients (HOG), Local binary patterns (LBP), etc. Abhishek et al. [5] have presented the Statistical technique for the feature extraction and then classified brain tumor by analyzing Brain MRI images using associative rules. The authors have taken the handicraft textual features as an input to the system for the classification of the brain tumor.

B. State-of-the-art architectures of CNN

AlexNet, VGG, GoogLeNet and ResNet are the popular architectures that were introduced for the image classification. Krizhevsky et al. [6] designed the first deep Convolutional Neural Network called AlexNet which is a 8 layer architecture composed of 5 convolutional layers and 3 fully connected layers. Then the University of Oxford presented their architecture called VGG which is the 19 layer architecture and made the improvements over AlexNet where the authors used multiple small size kernels to detect more complex features [7]. To utilize the computing resources Google introduced their model called GoogLeNet/inception. It cited the problem of computing efficiency and tried to design inception module that is efficient in the amount of computing. The inception modules are stacked on each other forming the 22 layer architectures [8]. To overcome the problem of vanishing gradient and training error that most deep neural networks faced during backpropagation, Kaiming et al. [9] introduced ResNet. It is a 152 layer architecture formed of residual module stacked over each other. All these architecture were introduced in ImageNet LSVRC for the classification of 1.2 million images into 1000 classification and emerged as winners as shown in Table I. They have huge memory and high computation power so the availability of requirements for these models is an important concern especially during training. The accuracy of the models is improved with the addition of layers making the architecture computationally intensive so there is a trade-off between accuracy and computation.

C. Hyperparameter tuning and Regularization

Tuning of hyperparameters such as learning rate, filter size, activation functions, iterations, hidden layers, hidden units help to improve the performance of deep networks without changing the architecture. L. N. Smith [10] has described a new model to get the best value of learning rate *(lr)* for the network which eliminates the need to find the value *lr* experimentally. The model is trained on small *lr* and then it is increased either exponentially or linearly at every iteration until it shows degrading performance. Instead of taking any fixed or exponentially decreasing value, the *lr* is cyclically varied within a range of values. The author has proposed the two triangular methods, 'triangular' and 'triangular2' with the minimum and maximum boundaries. The only difference is that min and max *lr* in triangular is same whereas in triangular2 after each cycle the difference between max and min is cut in half. The learning rate linearly increases from min to max and then linearly decreases from max to min. The cyclic *lr* has improved the accuracy of classification in fewer iterations. As the implementation of deep neural networks in many applications gained a lot of popularity, it faced one serious problem of high variance (overfitting) where the models get trained very well but show degrading performance during testing. Several regularization methods are used for preventing overfitting, among which the widely used are data augmentation, Lasso *(L1)*and Ridge *(L2)* regularization methods, and dropout. In data augmentation, the training data is increased enormously by making transformations in input images such as flip, crop, rotation [11]. *L1* and*L2* regularization methods are the standard ways to prevent overfitting. *L1* algorithm makes many weighted connections almost zero and creates the sparse networks by dropping these connections. *L2* algorithms are more considered about low weight values rather than creating sparse network which leads to less overfitting. The effective and simple regularization method is dropout. Hinton et al. [12] proposed the concept of dropout where the neurons were randomly dropped to prevent overfitting. The activation of neurons in the forward pass is temporally removed and weights are not updated on the backward pass which prevents the neurons to rely on other neurons to compensate for their mistakes. Hyperparameter tuning and Regularization are easy ways to overcome the most common problems of deep neural networks and are highly preferable.

D. Automatic extraction of features using deep learning

The extraction of distinct features is very difficult and need to be carefully designed so that the chances of missing out any distinct features is reduced. The deep learning techniques for medical image analysis eliminates the overhead of manually selecting features and hence improves the classification and the performance of the system. CNN extracts the features of input images with different lighting condition better than other classification methods [13]. Deep learning method like Faster Region-based Convolutional Neural Network (Faster R-CNN) [14] is used to train networks for the detection of cancer in lungs. The network is formed of two modules-Region Proposal Network depicts the region of interest and ROI classifier recognizes whether ROIs are nodule or not. The deconvolution layer is used in network to recover more fine-grained features of nodule because of its small size. RPN takes feature layer as input and outputs region of interest. Q. Song et al. [15] have taken 3 deep learning methods CNN, Deep Neural Network (DNN) and space autoencoder to classify nodules as malignant and benign on the LIDC-IDRI dataset. Among the three networks, CNN was successfull in selecting most distinct features of lung nodules in CT Scan images for classification of cancer and takes lead with accuracy of 84.16%.

E. Transfer learning and Ensemble learning used in medical image analysis

Transfer learning is a optimal solution when there is limited data available for training, where pre-trained weights of the standard deep network architectures are used as initialization weights. H.Chougrad et al. [16] have shown transfer learning is the good approach to start the learning process by reusing the pre-trained weights of pre-trained model (Inception-V3) as the initialization weights for their proposed model. The loaded weights were fine-tuned so that the model better fits the new Breast Cancer Digital Repository (BCDR-F03) dataset and hence improves the performance of the network for the better detection of breast cancer. Transfer learning with exponential decay of learning rate yielded an accuracy of 97.50% and AUC= 0.96. A. Esteva et al. [17] have also used pre-trained weights of Inception-V3 model for classification of skin cancer. The authors have got their results on the three tasks, the first is carcinoma which is the prevalent type of skin cancer. The second is the most dangerous type of skin cancer called melanoma and the third is dermoscopy images of melanoma. The pre-trained model is retrained with their ISIC dataset and the parameters are fine-tuned across all layers. Transfer learning with fine-tuning reduces the training time and improves the performance of model.

The ensemble networks were also proposed to maximize the performance of the network. In [18] the performance of GoogLeNet is improved by an ensemble of networks for pre-processing and decision fusion to classify microcalcification of a breast. In contrast with standalone models, ensemble models show better accuracy and are highly preferable. Codella et al. [19] have proposed ensemble models including deep residual networks, CNN, and fully convolutional U-Net architectures to segment the skin lesion, analyze the detected area and its surrounding tissue for recognition of melanoma.

F. New deep learning architectures

Many new architectures were designed which worked very well for medical images. K. J. Geras et al. [20] have proposed the Multiview Deep Convolutional Neural Network (MV-DCN) that takes the HD medical images for the classification of the breast cancer. The model is trained on 866,000 images and have classified images as BI-RADS 1 ("Assessment is incomplete"), BI-RADS 2 ("Negative") and BI-RADS 3 ("Benign findings"). S. Pereira et al. [21] have designed an automated system based on CNN for segmentation of tumor in the brain using MRI images. They have classified brain tumor into Low Grade Gliomas (LGG) and High Grade Gliomas (HGG) and have designed separate models for each. For HGG and LGG, the authors have used 11 and 9 layer architecture respectively. The proposed model is the winner of Brain Tumor Segmentation Challenge 2013 (BRATS 2013). S. Liu et al. [22] have proposed deep learning architecture (XmasNet) based on convolution neural network inspired by VGG for classification of prostate cancer lesions, using 3D multiparametric MRI image data provided by PROSTATEx challenge. P. Rao et al. [23] have trained CNN for lung cancer screening on Lung Images Database Consortium (LIDC) dataset. The proposed CanNet contains 2 convolution layer after the input layer followed by pooling layer, a dropout layer and a fully connected layer. Rotem et al. [24] have proposed Deep Convolutional Neural Network for Lung Nodule detection (DCNN). DCNN is trained to detect lung nodules in subvolumes of CT Scan images and used it to predict the location and boundary of lung nodules in unprocessed CT Scan images. J. Ma et al. [25] have proposed a hybrid CNN for the thyroid nodule diagnosis. It is the combination of 2 pre-trained CNN models, CNN 1 and CNN 2 with different convolution and fully connected layer. CNN 1 capture the ultra-fine low-level features and CNN 2 capture the complex features of the thyroid nodule.The feature maps of both the networks are fused and given as input to softmax classifier to detect thyroid nodule. N. Kumar et al. [26] have proposed the deep learning architecture for the detection of prostate cancer. The authors have used two CNN models, one for the detection of nuclei and second CNN model to classify them. Nima et al. [27] have taken 3 specialties in medical imaging application (cardiology, radiology, gastroenterology) and have done classification, detection, and segmentation and measured the performance of trained deep CNN from scratch and pre-trained CNN which is fine-tuned in a layer-wise manner. The better accuracy and performance of the deep learning techniques is not limited only to the standard architectures. Even newly designed deep learning frameworks yield captivated results, thus favors the use of these new architectures in many medical applications.

G. *Analysis of 3D volume medical images using deep learning*

CT scan and MRI produces hundreds of images for a single patient and analyzing all these images one by one is time-consuming. Therefore, 3D Computer Aided Design (CAD) technologies are used which take these CT Scan image slices and stack them into a concise 3D area. 3D-Convolution Neural Networks also performed tremendously well for 3D volume medical images. In the volumetric medical image analysis, 3D CNN has shown better results than 2D CNN [32]. Kingsley et al. [28] mentioned 3D CNN based on ResNet-101 for lung cancer detection in 3D CT scans and placed at 41st position in the KAGGLE DATA SCIENCE BOWL 2017 competition. The framework of the architecture is divided into four separate neural networks - nodule detector, malignancy detector, nodule classifier, patient classifier. The ResNet-101 is modified for nodule detection and malignant detection and ResNet-18 is modified for nodule classification. In [29] B. Erden et al. have designed a 3D-CNN for the detection of brain tumor. The authors have used U-Net for the segmentation of images and then fed it as input to 3D CNN. Albert et al. [30] have used modified U-Net to segment lung tissue trained on dataset LUNA16. The U-Net produces many false positive so the segmented output of U-Net is fed into 3D convolution neural network. Two CNN models, Vanilla 3D CNN and GoogLeNet based on 3D CNN are used to classify CT Scan as positive or negative for lung cancer.

The deep learning is used to learn about the fundamental process of tumor growth. In [31] the deep network is modelled to learn about cell invasion and mass effect for the prediction of tumor growth. They have shown their results on pancreatic tumor dataset. The idea of their model is to predict whether the voxel in current time point will have the tumor or not at the next time point. The input is the image patches that represent cell invasion and expansive growth information derived from multimodal imaging data. The output is either 1 (input patch will have the tumor at next time point) or 0 (input patch will not have the tumor at next time point). To take an advantage of invasion and expansion information, a number of ways for fusing invasion and expansion are studied which are Late Fusion, Early Fusion and End to End Fusion.

H. *Comparison of deep dearning with traditional techniques*

Deep learning techniques show favorable results when compared with traditional image analysis techniques. Harshita et al. [33] have proposed 9 layer CNN architecture for two applications called cancer classification and necrosis detection of stomach cancer from H&E stained images. The authors have compared their proposed CNN architecture with traditional methods - Gray level co-occurrence matrix, Gabor filter-bank responses, LBP histograms, gray histograms, HSV histograms and RGB histograms followed by machine learning method called the random forest. The proposed model is comparatively analyzed with standard architecture, ALexNet, for classification problems. RGB histograms followed by random forest among other traditional methods achieved the highest classification accuracy of 76.41%, AlexNet achieved 73.28% and the proposed architecture achieved 69.90%. For necrosis detection, the proposed architecture achieved the overall highest accuracy of 81.44%. In [34] the efficiency of the existing prostate CAD was compared with the proposed Deep Learning based Prostate-CAD (CAD_{DL}). CAD_{DL} attained 86% detection rate whereas CAD attained 80% detection rate.

I. *Effect of dataset on a model and cost function*

The deep learning architectures are trained on different datasets to make it more generalize. The models learn better with more data and acts as regularization method. In [35] Hakan et al. have used two deep learning architectures VGG and Resnet inspired by VGG16 and ResNet18 to detect the oral and cervix cancer. The authors have shown the variation of results with different dataset along with different architecture.

TABLE II
OVERVIEW OF DEEP LEARNING MODELS FOR THE DETECTION OF CANCER

Ref.	Architecture	Cancer	Image Size	Dataset	Performance metrics
[17]	Inception -V3	Skin	299x299	1SIC Archive, Edinburgh Dermofit library, Stanford Hospital, 129,450 images	Three-way accuracy = 72.1% ± 0.9% Nine-way accuracy = 55.4% ± 1.7%
[20]	MV-DCN	Breast	2600x2000	129,208 patients, 201,698 exams, 886,437 images	macAUC = 0.733 for 100% of data used for training.
[21]	CNN	Brain	33x33x4	BRAT 2013 : 65 MRIs & BRAT 2015 : 327 MRIs	Dice coefficient metric: BRAT 2013 = (0.88, 0.83, 0.77) & BRAT 2015 = (0.78, 0.65, 0.75)
[22]	XmasNet	Prostate	32x32	341 cases (DWI images+ADC maps+ Ktrans+T2WI images) 207144 images	AUC = 0.84
[23]	CanNet	Lung	128x128	1018 patients (LIDC-IDRI) 150 to 550 CT Scan images/patient	Test accuracy = 76.50%
[24]	DCNN	Lung	5x20x20	1018 patients (LIDC-IDRI) 150 to 550 CT Scan images/patient	sensitivity (true positive rate) = 78.9%
[25]	Hybrid CNN	Thyroid	255x255	15,000 ultrasound images	accuracy= 83.02% ± 0.72%
[26]	Hybrid CNN	Prostate	51x51x3 (N.D) & 101x101x3 (R.S.P)	220 cases (CPCTR)	AUC = 0.81
[29]	3D CNN & UNET	Brain	192x192x154	BraTS 2017: 285 brain volumes. 155 2D slices/volume	Dice Score = 0.71
[30]	3D CNN & UNET	Lung	256x256 (UNET) & 64x64x64x1 (CNN)	888 patients (LUNA), 2101 patients (KAGGLE), 100-400 CT Scan/patient, 512x512	accuracy = 80.5% (Vanilla 3D) & accuracy = 73% (GoogLeNet)
[35]	VGG / ResNet	Oral & Cervix	100x100x5	CerviSCAN, Herlev Dataset, oral dataset 1, oral dataset 2	avg accuracy = 83.06 (VGG), avg accuracy = 82.90 (ResNet)
[18]	Ensemble models	Breast	224x224	DDSM, 2620 samples	F1 Score = 94.5%
[19]	Ensemble models	Skin	128x128	ISIC, 1279 dermoscopic images	AUC = 0.843

The model is trained on CerviSCAN and Herlev dataset for cervix cancer detection and Oral Dataset 1 and Oral Dataset 2 for oral cancer detection. On cervical dataset, VGG and ResNet showed the accuracy of 84.20% and 84.45% respectively. On Herlev dataset, VGG and ResNet showed the accuracy of 86.56% and 86.45% respectively. For Oral Dataset 1 VGG and ResNet showed the accuracy of 80.66% and 78.34% respectively and Oral Dataset 2 VGG gained accuracy of 80.83% and ResNet 82.39% respectively. Besides softmax, SVM is also used as a cost function to measure the loss of the model. SVM gives the output for predicted class either in 0 or 1 where as softmax gives the output in some probability. It shows high probability for correct class and low probability for incorrect class. Compared to softmax, the SVM is not considered about the individual scores of the class. In [36] CNN is designed for the classification of H&E stained breast biopsy images into 4 and 2 classes. The four classes in which images are classified are normal, benign lesion, in situ carcinoma and invasive carcinoma and the two classes are carcinoma and non-carcinoma. The SVM is used as classifier where the features extracted by CNN are given as input and classified into benign or malignant.

J. Capsule Network

Convolutional Neural Network are translation and spatial invariant. When the object in an image is altered in position or rotation it can still classify that object but does not predict any additional information of alternation. Hilton et al. [37] proposed the implementation of the idea of CapsNet. A CapsNet is basically a neural network that performs inverse graphics and it is composed of many capsules as shown in Fig. 2. A capsule is a function that predicts the presence and instantiation parameters of a particular object at a given location. A capsule is a group of neurons whose output is the activity vector that represents the instantiation parameter of the entity such as an object or object part. Length of the vector represents the probability of the existence of that entity and its orientation represent that parameter. The authors have trained their network on MNIST dataset. They have used an iterative *'routing by agreement'* mechanism which means the capsule at the low level will send its output only to the neurons at the high level which has an activity vector with a big scalar product. By big scalar product we mean the probability of having an accurate output at the last layer will be through these neurons at high level. The Capsnet got the low test error (0.25%) on a 3 layer network which was previously achieved by deep networks with many layers.

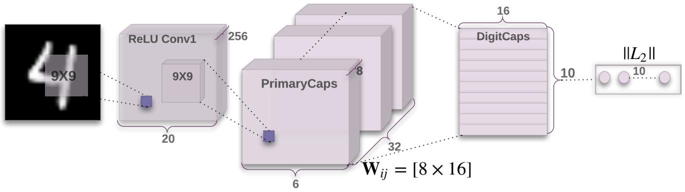

Fig. 2. Capsule Network by Hinton et al. [37] in 2017

III. Characteristics of new deep learning architectures for detection of cancer

Different deep learning architectures were used for the analysis of medical images for the detection of the various cancers where each architecture takes different size of images as input and the performance of the architecture is measured by different performance metrics as shown in Table II.

IV. Conclusion

The analysis of medical images such as X-Rays, CT Scans and MRIs is a difficult task because of the increase in digital medical data every year which requires high potential analysis techniques. Deep learning is in fame because of its phenomenal classification of millions of images. It came in collaboration with the medical imaging and performed exceptionally well. We have highlighted the use of deep learning techniques for the detection of cancer. The state-of-the-art such as ResNet, GoogLeNet or VGG are used for medical image analysis. Also, new architectures were designed that performed better for classification of cancer. 3D deep networks were introduced for 3D volumetric medical image analysis detecting the most discriminating features that classify the number of diseases.

The ensemble of CNN models is also used to improve the predictive power of the model for better prediction of cancer. Transfer learning with fine-tuning of parameters is incorporated in medical image analysis increasing the performance of pre-trained models for better classification and reducing the training time. Regularization methods help to overcome the problem of overfitting and tuning of hyperparameters improve the performance of the deep neural networks without making any kind of changes in the architecture which is very effective and feasible. The CNN models have worked a lot in medical image analysis and performed comparatively better than the traditional image processing techniques. CapsNet has achieved the desirable accuracy by only the three layer architecture which is usually achieved by deep layer networks. We expect that medical image analysis will improve more with the use of CapsNet. Deep learning is revolutionizing the healthcare with its extraordinary capabilities making the diagnosis and detection more accurate and faster. All these emerging technologies and new fascinating advancements in medical sciences contribute to the better health.

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