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A Review of Deep Learning Methods Applied to Ocular Diseases Recognition and Detection

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Abstract: ***Artificial intelligence is having an important effect on different areas of drug, and ophthalmology isn't the exception. In particular, deep literacy styles have been applied successfully to the discovery of clinical signs and the bracket of optical conditions. This represents a great eventuality to increase the number of people rightly diagnosed. ophthalmology, deep literacy styles have primarily been applied to eye fundus images and optic consonance tomography. On the one hand, these styles have achieved outstanding performance in the discovery of optical conditions similar as diabetic retinopathy, glaucoma, diabetic macular degeneration, and age- related macular degeneration. On the other hand, several worldwide challenges have participated big eye imaging datasets with the segmentation of part of the eyes, clinical signs, and optical judgments performed by experts. In addition, these styles are breaking the smirch of black-box models, with the delivery of interpretable clinical information. This review provides an overview of the state-of-the- art deep literacy styles used in ophthalmic images, databases, and implicit challenges for optical opinion.***
Keywords: Clinical signs; optical conditions; optical dataset; deep literacy; clinical opinion

I. INTRODUCTION

Iris cataract tumours are the most dangerous tumours in the eye, commonly known as ‘eye tumours’.Most cataracts develop when aging or injury changes the tissue that makes up eye’s lens. Protiens and fibres in the lens begin to break down, causing vision to become hazy or cloudy. Some inherited genetic disorders that cause health problems can increase your risk of cataracts. The term ocular is used with tumour to represent that it is accompanied with eye. It can be intraocular, which means inside the eye or extra-ocular which means that it affects the outside part of the eye. The most common types of diseases are detected are cataract, diabetic retinopathy, redness level. Some other tumours related to the eye are Lacrimal Gland Tumour, lid tumour, etc. The exact cause of this disorder is not known, but certain risk factors have been noticed. The disorder is seen more often in people who have light eye colour . Age, certain inherited skin disorders, exposure to ultraviolet (UV)light, certain genetic mutations etc are also considered as thereasons for eye tumours. The eye tumour can be spread and shall affect the vision.

Routine checkups are the best methods for diagnosing the tumour. Ophthalmoscope is commonly used to diagnose. Ultrasound, Fluorescein angiography test OCT, Semiconductor Detectors are the other common methods to diagnose. Needle biopsy is rarely used for diagnosis. CT to age, health state, suspected disease, symptoms and pastexamination records. Cytogenetics and gene expression profiling are used to collect more information about prognosis. Iris tumours are most common eye tumours and it is classified into different types. For earlier detection of thesetumours, generalised procedure is needed to diagnosethe abnormality.

The two most commonly used therapeutic procedures are surgery or radiation therapy. In Radiation therapy damage produced in the tumour cells causes them to die and slowly shrink. The most common radiation therapies are endocrine therapy, brachytherapy, or sealed source radiotherapy 5. Shrinking of the tumour region can be completely cured with local therapy. The local therapy consists of laser photocoagulation, cryotherapy, thermotherapy, Plaque radiotherapy etc. Laser photocoagulation is the primary therapy with xenon or argon arc. This coagulates all blood supply to the tumour and it can control 70% of the abnormality. Cryotherapy commonly treated for small tumours. The procedures for chemotherapy start with cryotherapy as a preparation step. Thermotherapy is the method of applying heat to the affected area using ultrasound, microwaves, or infrared radiation.

Ophthalmology is a branch of medical science that investigates the disorders of the eye. Bio medical imaging software is the efficient tool for ophthalmologists in diagnosing eye diseases. These imaging techniques also help them in surgical treatment. Most of the image diagnosing machines are working with the principle of machine learning.Fundus and OCT image records can reveal the symptoms of diabetes. Many cameras are available now for capturing iris regions of the eye. These images are used both forbiomedical and biometric applications. The eye tumour examinations can be undertaken with the pictures. More research works should come across in the field of ocular disease detection detection

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Early ocular disease detection is an economic and effective way to prevent blindness caused by diabetes, glaucoma, cataract, age-related macular degeneration (AMD), and many other diseases. According to World Health Organization (WHO) at present, at least 2.2 billion people around the world have vision impairments, of whom at least 1 billion have a vision impairment that could have been prevented1. Rapid and automatic detection of diseases is critical and urgent in reducing the ophthalmologist's workload and prevents vision damage of patients. Computer vision and deep learning can automatically detect ocular diseases after providing high-quality medical eye fundus images. In this article, I show different experiments and approaches towards building an advanced classification model using convolutional neural networks written using the TensorFlow library.

II. DATASET

Ocular Disease Intelligent Recognition (ODIR) is a structured ophthalmic database of 5,000 patients with age, color fundus photographs from left and right eyes, and doctors' diagnostic keywords from doctors. This dataset is meant to represent the ''real-life'' set of patient information collected by Shanggong Medical Technology Co., Ltd. from different hospitals/medical centers in China. In these institutions, fundus images are captured by various cameras in the market, such as Canon, Zeiss, and Kowa, resulting in varied image resolutions. Annotations were labeled by trained human readers with quality control management2. They classify patients into eight labels including normal (N), diabetes (D), glaucoma (G), cataract (C), AMD (A), hypertension (H), myopia (M), and other diseases/abnormalities (O).

After preliminary data exploration I found the following main challenges of the ODIR dataset:

1) Highly unbalanced data. Most images are classified as normal (1140 examples), while specific diseases like for example hypertension have only 100 occurrences in the dataset.
2) The dataset contains multi-label diseases because each eye can have not only one single disease but also a combination of many.
3) Images labeled as "other diseases/abnormalities" (O) contain images associated to more than 10 different diseases stretching the variability to a greater extent.
4) Very big and different image resolutions. Most images have sizes of around 2976x2976 or 2592x1728 pixels.

All these issues take a significant toll on accuracy and other metrics. In recent times, the discovery of clinical signs and the grading of optical conditions have been considered engineering grueling tasks. In addition, worldwide experimenters have published their styles and a set of EFIs and OCTs databases with different optical conditions, population, accession bias and image resolution. The available optical datasets for each optical complaint, the type of optical image and the study population are presented in Table 1.

III. PERFORMANCE METHODS

Deep learning approaches have shown astonishing results in problem domains like recognition system, natural language processing, medical sciences, and in many other fields. Google, Facebook, Twitter, Instagram, and other big companies use deep learning in order to provide better pplications and services to their customers. Deep learning approaches have active applicatio s using Deep Convolutional Neural Networks (DCNN) in object recognition, speech recognition, natural language processing, theoretical science, medical science, etc.
In the medical field, some researchers apply deep learning to solve different medical problems like diabetic retinopathy, detection of cancer cells in the human body, spine imaging and many others. Although unsupervised learning is applicable in the field of medical science where sufficient labeled datasets for a particular type of the disease are not available. In particular, the state-of-the-art methods in ocular images are based on supervised learning techniques.

A. Performance Metrics in Deep Learning Models

The performance comparison of deep learning methods in classification tasks is performed by the calculation of statistical metrics. These metrics assess the agreement and disagreement between the expert and the proposed method to grade an ocular disease [35],[62],[74]. The performance metrics used in state-of-the-art works are presented in Equations (1 - 7) as follows:

$$Area\ under\ the\ curve\ (AUC) = \frac{\sum Rank(+) - |+| * \frac{(|+|+1)}{2}}{|+| + |-|} \quad (1)$$

$$Accuracy = \frac{TP + TN}{TP + TN + FP + FN} \quad (2)$$

$$Sensitivity = \frac{TP}{TP + FN} \quad (3)$$

$$Specificity = \frac{TN}{TN + FP} \quad (4)$$

$$Precision = \frac{TP}{TP + FP} \quad (5)$$

$$f - score = \frac{2 * Precision * Recall}{Precision + Recall} \quad (6)$$

$$Kappa\ coefficient = \frac{p_o - p_e}{1 - p_e} \quad (7)$$

where,
TP = True positive (the ground-truth and predicted are non-control class)
TN = True Negative (the ground-truth and predicted are control class)
FP = False Positive (predicted as a non-control class but the ground-truth is control class)
FN = False Negative (predicted as control class but the ground-truth is non-control class)
po = Probability of agreement or correct classification among raters.
pe = Probability of chance agreement among raters.

IV. DEEP LEARNING METHODS FOR DIAGNOSIS SUPPORT

A. *Dl Methods using Eye Fundus Images*

The state-of-the-art DL methods to classify ocular diseases using EFIs are focused on conventional or vanilla CNN and multi-stage CNN. The most common vanilla CNN used with EFIs are the pre-trained inception-V1 and V3 models on the ImageNet database (http://www.image-net.org/). The inception-V1 is a CNN that contains different sizes of convolutions for the same input to be stacked as a unique output. Another difference with normal CNN is that the inclusion of convolutional layers with kernel size of 1x1 at the middle and global average pooling at the final of its architecture [79]. On the other hand, inception-V3 is an improved version batch normalization and label smoothing strategies to prevent overfitting [91].

[94] used the U-Net model proposed by [92] to segment the retinal vessel from EFIs. Then, two new datasets were created with and without the vessels to be used as inputs in the inception-V1. This method obtained an AUC of 0.9772 in the detection of DR in the DRIU dataset. [96] and [98] proposed a patch-based model composed of pre-trained inception-V3 to detect DR in the EyePAC dataset. [98] used a private dataset with segmentations of clinical signs to classify an EFI into normal or referable DR with a sensitivity of 93.4 % and specificity of 93.9 %. The ensembled of four inception-V3 CNN by [96] reached an accuracy of 88.72 %, a precision of 95.77 % and a recall of 94.84 %.

The multistage CNN is centered first on the detection of clinical signs to sequentially grade the ocular disease. [95] located different types of lesions to integrate an imbalanced weighting map to focus the model attention in the local signs to classify DR obtaining an AUC of 0.9590. [97] used a similar approach to generate heat maps with the detected lesion as an attention model to grade in an image-level the DR with an AUC of 0.954. [99] uses a four-layers CNN as a patches-based model to segment exudates and the generated exudate mask was used to diagnose DME reporting an accuracy of 82.5 % and a Kappa coefficient of 0.6. Then, [104] proposes a three-stage DL model: optic and cup segmentation, morphometric features estimation and glaucoma grading, with an accuracy of 89.4 %, a sensitivity of 89.5 % and a specificity of 88.9 %. Finally, [101] proposed a model to segment optic disc and cup and calculate a normalized cup-discratio to discriminate healthy and glaucomatous optic nerve of EFIs. Table 2 presents a brief summary of DL methods in eye fundus images used to support an ocular diagnosis.

V. DISCUSSION

This review reports the deep learning state-off-the-art works applied to EFIs and OCT for ocular diagnosis as presented in Tables 2 and 3. The main DL methods in the detection of ocular diseases using EFIs are focused on the fine-tuning of pre-trained CNNs such as Inception V1 [94] and Inception V3 [96]. In addition, the pre-trained CNNs applied to OCT obtained an outstanding performance as reported with pre-trained ResNet [35],[105], VGG-16 [111] and Inception V3 [74]. Thus, the feature extraction stage performed by CNNs using a non-medical domain dataset from ImageNet is enough to discriminate healthy and unhealthy patterns from ocular images. On the other hand, the best CNN models using OCT volumes as input are customized models with two or three stages. In particular, these DL models used two or more ocular medical datasets reported in Table 1 to perform the feature extraction of local signs, added to a classification stage for grading the ocular diseases as reported for EFIs in [95],[97],[99]-[103] and for OCTs in [106]-[109].

The number of free public available datasets contributes to the design of new DL methodologies to classify ocular conditions as reported in Table 1. However, the use of a private dataset limits the comparison among performance metrics reached by DL methods [74],[98],[110]-[111]. The replication of studies reported by [98] and [110] have been criticized for the lack of information related to the description of the method and the hyperparameters used [113]. The use of public repositories as GitHub (https://github.com/) to share datasets and codes is still a need. Nowadays, the growing interest of big technology companies and medical centers to create open challenges has increased the number of ocular datasets such as the DR detection by Kaggle [53],[84], the blindness detection by the Asia Pacific Tele-Ophthalmology Society (APTOS) [54] and iChallenge for AMD detection by Baidu [34]. These new datasets contain diverse information related to acquisition devices, image resolution, and worldwide population. Moreover, DL techniques are leveraging the new data to the design of new robust approaches with outstanding performances as reported in Tables 2 and 3.

The lack of validation of DCNN models with real-world scans or fundus images is still a problem. We found a couple of methods validated with ocular images from medical centers [96], [108]-[111]. However, the number of free public real-world ocular images is limited to five sets of images [31],[46],[53]-[54],[74]. The clinical acceptance of the proposed DCNN models depends critically on the validation in clinical and nonclinical datasets.

VI. CONCLUSIONS

Deep Literacy styles are new ways that descry and classify different abnormalities in eye images with great eventuality toeffectively optical complaint opinion.These styles take advantage ofa large number of available datasets with different reflections of clinical signs and optical conditions to perform the automatic point birth thatsupports medical decision timber

Ocular disease	Dataset	Dataset description
DR	[47]	40 eye fundus images with a resolution of images are 768 x 584 pixels. The dataset contains 7 images graded by experts as mild DR and 33 images as normal.
	[48]	130 eye fundus images with 110 DR and 20 normal images. The images labeled as DR contain the segmentation of clinical signs: hard exudates, soft exudates, microaneurysms, hemorrhages, and neovascularization.
	[49]	89 eye fundus images where 84 images have mil DR and 5 images labeled as normal.
	[50]	100 digital color fundus images with microaneurysms in all the images. This dataset was randomly split into training and test datasets with 50 images.
	[51]	28 eye fundus images with two blood vessel segments performed by experts.
	[52]	Two subsets: a set of 47 eye fundus images with the segmentation of exudates and 35 images without lesions labeled as normal. The second set has 148 images with microaneurysms and 233 images labeled as normal.
	[53]	Two subsets: the training set has 35126 and the test set has 53576. The images were labeled as normal, mild, moderate, severe and proliferative DR.
	[54]	13000 images with normal, mild, moderate, severe and proliferative DR.
DR, Glaucoma	[55]	49 eye fundus images with the optic head segmentation and the grading of DR and glaucoma.
	[56]	45 eye fundus images with 15 healthy, 15 DR and 15 glaucomatous subjects. The images have the detection and segmentation of clinical signs provided by experts.
DR, DME	[26]	1200 eye fundus images with DR and DME labels performed by an expert.
	[23]	516 images with a resolution of 4288x2848 pixels with the grading of DME and DR performed by experts.
DR, AMD	[57-58]	400 eye fundus images and 400 black and white masks with blood vessel annotations.
	[59-60]	143 color fundus images with a resolution of 768x576 pixels. The images were grading as 23 AMD, 59 DR, and 61 normal images.
	[61]	500 OCTs with normal, macula hole, AMD, central serous retinopathy and DR.
Glaucoma	[62]	110 color fundus images with optic nerve head segmentation. The images were labeled as 26 glaucomatous and 84 with eye hypertension.
	[63]	650 eye fundus images with the classification of glaucoma condition.
	[64]	40 color images with the blood vessels, optic disc, and arterio-venous reference.
	[31]	783 images with glaucomatous, suspicious of glaucoma and normal conditions.
	[65]	258 eye fundus images with 144 normal and 114 glaucomatous subjects.
	[66-67]	101 images with optic disc and optic cup segmentation and glaucoma condition.
	[68]	760 retinal fundus images with glaucoma labels.
	[69]	1200 eye fundus images with optic disc and cup segmentation with normal and glaucoma conditions.
	[32]	1110 scans where 263 were diagnosed as healthy and 847 with primary open-angle glaucoma (POAG).
AMD	[70]	206500 eye fundus images with AMD and non-AMD conditions.
	[34]	1200 eye fundus images with early AMD and non-AMD conditions.
	[35]	385 OCTs with 269 AMD and 115 normal subjects. Each OCT volume has 100 B-scan with a resolution of 512x1000 pixels.
	[71]	15 OCT volumes with the retinal layer segmentation performed by an expert. The database was labeled with AMD condition.
DME	[72]	169 eye fundus images with mild, moderate and severe DME.
DME, AMD	[27]	45 OCTs with 15 AMD, 15 DME, and 15 normal subjects. Each OCT volume has 100 B-scan with a resolution of 512x1000 pixels.
	[73]	148 OCTs as follows: 50 DME, 50 normal and 48 AMD subjects.
	[74]	109309 scans of subjects with DME, drusen, choroidal neovascularization and normal conditions.
DME, AMD, DR	[24]	75 OCTs labeled as 16 normal, 20 DME and 39 DR-DME. The OCT volume contains 128 B-scans with a resolution of 512x1024 pixels.
DR, AMD, Glaucoma	[46]	231806 OCTs and eye fundus images with the labels of glaucoma, DR and AMD.

Table 1 A summary of free public optical datasets with optical conditions graded by experts, dataset names and dataset descriptions,

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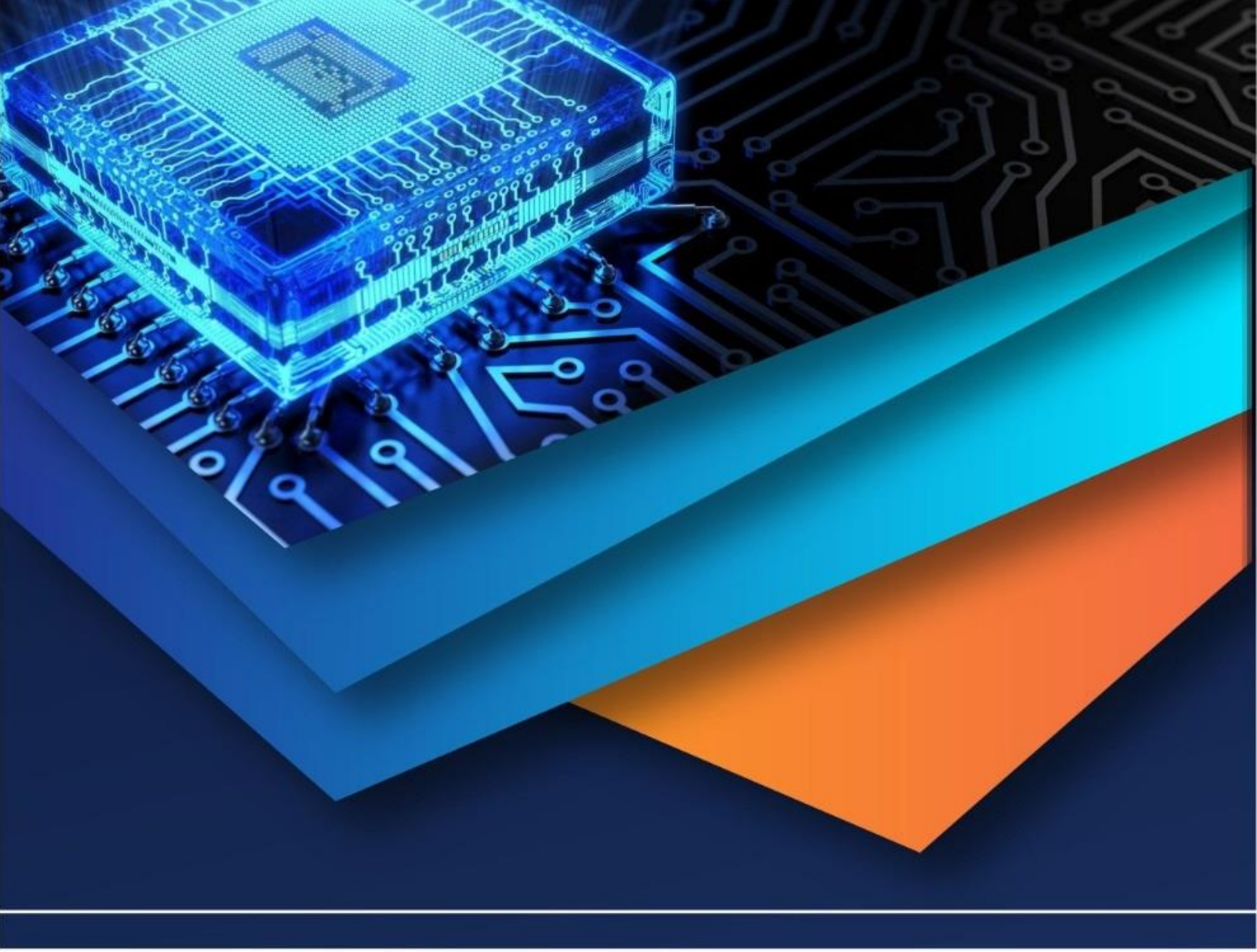

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