Diagnosis of Diabetic Retinopathy Using Computational Techniques

Aparna Deshmukh
Asst. Professor,
Department of Biotechnology,
Thakur College, Mumbai, India
drasdeshmukh@gmail.com

Mihir Deshmukh
Final Year Student of B.E. (ENI)
Birla Institute of Technology,
Pilani, Rajasthan, India
mihirsdeshmukh10@gmail.com

Abstract : Retinopathy is one of the complications of diabetes mellitus. Diagnosis of retinopathy is based on imaging of fundus by ophthalmoscopy. With the recent advancement in image analysis techniques, many machine learning and artificial intelligence based approaches have emerged as potential tools for detection and quantification of retinopathy. A study was undertaken to compare and analyse the computational techniques on the basis of sensitivity, specificity and accuracy. This article presents a review of the reported promising computational techniques.

Index Terms - Diabetic retinopathy, fundus imaging, CNN

I. INTRODUCTION

Diabetes mellitus, a chronic disorder in which function or production of insulin hormone is impaired results in hyperglycemia, and affects carbohydrate metabolism and other metabolic biochemical pathways. Long standing Diabetes mellitus is associated with multiple complications with varied severity. One of the complications is diabetic retinopathy (DR) caused by impaired angiogenesis and vascular changes. Severe retinopathy can lead to loss of vision and is a major cause of adult blindness. As per WHO report, estimated number of patients with diabetes mellitus by 2030 is 366 million amongst which 75% will have some form of diabetic retinopathy (WHO,2005).

Early accurate detection and appropriate treatment can significantly reduce the risk of vision loss in patients with diabetic retinopathy. Diagnosis of diabetic retinopathy involves fundus photography which is analysed either through direct visual screening by medical experts or assisted by computer aided tools. Although, detection of retinopathy by clinical experts is not a cumbersive task, precise determination of severity of the vascular damage is subject to special expertization. With the recent advancement in image analysis techniques, many machine learning and artificial intelligence based approaches have emerged as potential tools for fundus photography based detection and quantification of retinopathy. We present a review of the comparative analysis of the recent computational techniques for assessment of severity of retinopathy.

II. METHODOLOGY

For the present study, research papers published during last five years (2013-2018) in various journals was selected on the basis of study universe, dataset variables and analytical techniques. Comparison of the reported computational techniques was carried out on the basis of sensitivity, specificity, and AUC. The details of the parameters under study are as follows.

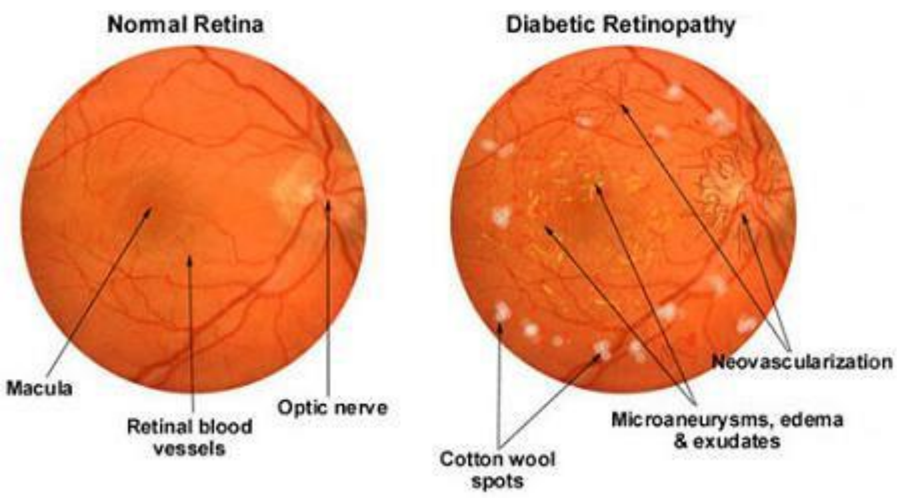
2.1 Symptoms of retinopathy presented in fundus photography

Retinal vascular damage can be detected in fundus image in the form of microvascular leakage and microvascular occlusion. The pathological changes in retinal vasculature are characterised as the following symptoms:

1. **Microaneurysm:** Early detectable signs characterised by outpouching of capillaries
2. **Exudate:** Leakage of proteins/lipoproteins from abnormal vessels
3. **Edema:** Swelling
4. **Hemorrhages:** Rupture of weakened capillaries presented as small red dot-like areas
5. **Cotton wool spots:** White lesions caused by microinfarcts in the retinal nerve fibres due to soft exudates which appear in advanced stages of nonproliferative retinopathy.
6. **Neovascularization:** Areas of angiogenesis characterised by formation of new blood capillaries

The symptoms have been depicted in Fig.1.

Figure 1. Symptoms of retinopathy presented in fundus photography



Source : https://www.medfordretinacare.com/2016/10/diabetic-retinal-exam/

2.2 Diabetic Retinopathy severity scale

Diabetic retinopathy can be categorized as non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). The symptoms of non-proliferative diabetic retinopathy include microaneurysms, hemorrhages, exudates and microinfarcts. Proliferative diabetic retinopathy is an advanced stage associated with neovascularization, vitreous hemorrhage and other complications like glaucoma and retinal detachment. Severity of diabetic retinopathy can be assessed on the basis of presentation of symptoms as depicted in **Table 1.**

Table 1. Diabetic Retinopathy severity scale*

Stage Number	Stage Name	Symptoms
0	No apparent retinopathy	No abnormalities
1	Mild nonproliferative diabetic retinopathy	Microaneurysms only
2	Moderate nonproliferative diabetic retinopathy	More than just microaneurysms but less than severe nonproliferative diabetic retinopathy
3	Severe nonproliferative diabetic retinopathy	Any of the following: ● more than 20 intraretinal hemorrhages in each of 4 quadrants; ● definite venous beading in 2 quadrants; ● Prominent intraretinal microvascular abnormalities in 1 Quadrant And no signs of proliferative retinopathy
4	Proliferative diabetic retinopathy	One or more of the following: neovascularization, vitreous/preretinal hemorrhage

Source : American Academy of Ophthalmology

2.3 Metrics

The papers reviewed in this study use standard metrics of sensitivity, specificity and AUC (area under curve).

Sensitivity (recall) measures actual positives, correctly identified=$TP/(TP + FN)$
Specificity measures actual negatives, correctly identified =$TN/(TN + FP)$
Accuracy measures all correctly identified results from all the predictions =$(TP + TN)/(TP + FP + TN + FN)$
Where TP = true positive, TN = true negative, FP = false positive, FN = false negative results.

AUC (area under curve), a tool to measure the trade off between precision and recall, is defined as the area under the curve of the receiver operating characteristic of sensitivity *vs* 1- specificity.

III. RESULTS & DISCUSSION

Recent studies using computer assisted analysis of retinopathy have focused on automated grading based on the symptoms presented in fundus photography. The table 2 given below summarizes the reported research work on automated grading of severity of diabetic retinopathy using Deep Learning and Image Processing methodologies. It also includes results of the studies on benchmark accuracy of commercial devices existing in the market.

Table 2 Computational Techniques Reported for Diagnosis of Diabetic Retinopathy

2.a Deep Learning Techniques

Sr. No.	Computational Technique used	Technical Specifics of Methodology	Dataset/ Metric used	Sensitivity	Specificity	Accuracy	AUC	Reference
1	CNN	Transforming retinal photos to entropy images	Kaggle	73.24%	93.81%	86.10%	0.92	Lin *et al.* 2018
2	CNN, Transfer Learning on imagenet trained network	Adjudication, using high resolution images improved results	Training Dataset: 16M images custom dataset	97.10%	92.30%	-	0.954	Krause *et al.* 2018
			Test Dataset: Eye PACS 2	97.10%	91.70%	-	0.986	
3	Visualization of CNN predictions	Heat maps using back propagation on CNN	Kaggle	-	-	-	0.955	Quellec *et al.* 2017
4	CNN, Transfer Learning on imagenet trained network	GoogleLeNet, concatenated images increase FOV	Manually clicked images	-	-	81%.	-	Takahashi *et al.*2017
5	CNN	Used similar network for glaucoma	Various datasets for training and validation	90.50%	91.60%	-	-	Wei Ting *et al.* 2017
				100%	91.10%	-	-	
6	CNN	Classification in 2 classes, healthy and unhealthy using decision tree	MESSIDOR 2 and E-Ophtha	94%	98%	-	0.97	Gargeya & Leng 2017
7	CNN, Transfer Learning on imagenet trained network	Inception-v3 trained on fundus images	EyePACS-1	90.3%*/ 97.5%	98.1%*/ 93.4%	-	0.991	Gulshan *et al.* 2016
			Messidor-2	87.0%*/ 96.1%	98.5%*/ 93.9%	-	0.99	

* indicates the best sensitivity/specificity values provided by the authors, **-** indicates values not available

2.b.Image Processing

Sr. No.	Computational Technique used	Technical Specifics of Methodology	Dataset/ Metric used	Sensitivity	Specificity	Accuracy	AUC	Reference
1	Image processing, Machine learning	Dimensionality reduction	ROC competition database	96%	92%	-	-	Kumar *et al.* 2018
2	Image processing, Machine learning	Classification of texture feature by performing a variation of Local Binary Pattern	Diaret DBO	-	-	96%	-	Abdillah, 2017

2.c.Other works on testing/validating/conducting statistical trials on existing devices/softwares

Sr. No.	Computational Technique used	Technical Specifics of Methodology	Dataset/ Metric used	Sensitivity	Specificity	Accuracy	AUC	
1	IDx-DR	ICDR scale & custom database with wide demographic data	87.2%	90.7%	-	0.980	Abramoff *et al*, 2018	
2	IDx-DR	ICDR scale & EURODIAB Database	91%	84%	82.85%	0.94	Van der Heijden 2017	
3	IDx-DR by Eyenuk, Inc.	ICDR scale & custom database consisting of 1661 Ultra Wide Field images	91.7%/* 90.3%	50.0%/* 53.6%	-	0.873/* 0.851	Wang *et al*, 2017	

* indicates the best sensitivity/specificity values provided by the authors, - indicates values not available

The study reveals that computational techniques are useful for grading of DR with variable accuracies. Accuracy can be improved using certain methodologies e.g. Lin *et al.* used deep learning for analysis of fundus photographs by transforming retinal photos to entropy images to improve accuracy. Krause *et.al.* have elaborated on the use of reference standards by ophthalmology experts for correcting machine grader variability in DR assessment. Their work projects that the use of adjudication yields more reliable outputs with higher accuracy in measuring severity of diabetic retinopathy.

Deep learning, as a technique, relies on extraction of relevant information by the network without manual inputs. Majority of the computational work in this domain use CNNs. It is shown that use of transfer learning, either on imagenet database or other diabetic retinopathy related database can improve the prediction accuracy of the network as compared to training it from scratch. Different methods use adaptations of networks like ResNet (Kaiming He *et al.* 2015), Inception (Szegedy *et al.* 2015), to obtain improvements in predictions. A typical pipeline in this category involves image preprocessing, feature extraction and classification. Various techniques for preprocessing include removal of noise, increase of contrast and sharpening of image. Since the ICDR scale establishes presence of various different features such as grading microaneurysms or exudates with different levels of severity, these approaches rely on their detection. This is followed by classification using machine learning techniques like SVM (Suykens & Vandewalle, 1999), Random Forests (Leo Breiman, 2001) or neural networks (Hansen, 1990) depending on the dataset.

The ground truths of severity are obtained by labels marked by trained ophthalmologists. The severity labels are obtained by the characteristics defined in Table 1. Deep learning systems use an end to end, supervised, CNN based detection network with little or no pre-processing. Non deep learning methods involve detection of the features mentioned in the severity scale and allotment of severity. Presence of high accuracy devices like IDx-DR show that there is a demand for automated screening aids for ophthalmologists.

IV. CONCLUSION

A large number of real world problems can be solved by Deep learning (LeCun *et al.* 2015). Diagnosis of diabetic retinopathy is one such area in which advances of machine learning and deep learning have contributed immensely. This review of recent research papers on diabetic retinopathy highlights that use of CNNs gives higher accuracy when the patterns to be found are not known beforehand. Image preprocessing and image enhancement techniques have shown to improve accuracy in deep learning based grading of severity of diabetic retinopathy.

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