Automated Techniques for Detection and Classification of Diabetic Macular Edema: A Review

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***Abstract*—Diabetic Macular Edema is the main cause of vision loss in diabetic patients caused by the accumulation of fluid in the macular region of retina. Detecting it at an early stage is a herculean task and requires great expertise and consumption of time. Many automated techniques developed to do so were analyzed in this study. Moreover, a fine survey of pre-processing techniques, feature selection, feature extraction, Machine Learning (ML) techniques and the data sets used for its training and testing was conducted. Many automated techniques in that matter have been able to achieve high accuracy in detection as well as classification of DME. Optical Coherence Tomography (OCT) stands out to be more effective and better result yielding than others for the detection and classification of DME**

***Keywords*—Automated techniques, DME Detection, DME Classification, OCT, Feature Selection, Feature Extraction**

I. Introduction

MACULAR Edema is the main cause of visual loss in diabetic patients. Diabetic Macular Edema causes the patient to lose the central focus of the vision and in extreme cases; blindness. Fig. 1 shows the comparison between the sight of a normal eye and that of a patient of DME. The history of DME dates back to 1850 when ophthalmoscope was invented by Helmholtz. Jaeger, in 1856, was the first to discover DME in a patient with Diabetes. DME was recognized as a clinical entity after 1875. Diabetic Macular Edema is caused by the accumulation of fluid in the macular region of retina. This accumulation of fluid causes the macula to thicken and swell. This swelling then distorts the cones in the region that produces central vision and thus the central vision of the patient is lost.

Fig.1. Comparison of Normal vision vs. that of DME

Diabetes is thought to be the common cause of Macular Edema which is considered to be a major symptom of Proliferative Diabetic Retinopathy (PDR). Diabetes is one of the most prevalent diseases in developed countries estimated to affect 8.5% of the European population according to recently collected data [4]-[1] and a diabetic patient tends to have chances to have DME after 10 years of the disease. In diabetic patients, blood retinal barrier becomes weak due to changes in retinal vessels which causes the fluid to leak into retinal layer which causes it to swell and thicken up to 2dd (disc diameter) of the center of macula. Earlier diagnosis of DME in the matter is an issue that needs considerate attention. After 20 years of disease, nearly all patients with type 1 and 60% of the patients with type 2 diabetes have some degree of retinopathy. Diagnosis of DME can be done automatically based on the features to be taken as base and the technique to be used.

A lot of work has been done for the automated detection and classification of Diabetic Macular Edema. Different approaches to develop an accurate system analysis have yielded better results. As manual detection and prediction of DME is a very tricky and delicate matter and requires perfect expertise and a slight misdiagnose can lead to hectic problems for the patient. So, to surpass this limitation, a lot of work has been done in this matter to automate the techniques to detect DME. Automated DME detection has been achieved using 3-D thickness maps of sub-retinal layers [1], Image segmentation to detect bubble of blood in Retinal Nerve Fiber Layer (RNFL) [5], localization of cysts in cystoid region using solidity, mean and maximumpixel value of the negative OCT image [6], Using spatial distribution and empirical linear transformation to achieve Fluorescein Leakage Maps (FLM) [7], Using filter bank, feature extraction to detect Exudates on retina [8], Region based detection of lesions in macular region, independent of optic disc detection [9], Using Texture features [10]. Similarly, work done for the classification of DME includes Classification using SD-OCT Volumes based on local binary patterns(LBP) [2], Classification based on the segmentation and processing of Outer Nuclear Layer (ONL) [4], Using SVM classifier [10], classification between AMD and DME based on detection of bubbles or drusen in retinal layers [5], using Gaussian Mixture Model in [8]. OCT is considered to be an effective technique for the classification and detection of DME. As it has been developed earlier, the amount of information given by OCT demonstrates that macular edema is a complex clinical entity with various morphology and gravity, and disclaimed the limitations of simple “clinic” definition [3]. Fig. 2 shows the OCT image comparison of normal and effected eye.

II. TYPES OF DME

Diabetic Macular Edema can be classified into two types; Focal and Diffuse. Both of them are to be taken differently as treatment for both is different. Foci of vascular abnormalities, primarily micro aneurysms which tend to leak fluid, are mainly the cause of Focal Macular Edema whereas Diffused Macular Edema is caused by the dilation of retinal capillaries in the retina. Focal Macular Edema is basically associated with hard exudates rings which are the result of leakage from micro aneurysms whereas diffused macular edema results from the breakage of blood-retinal barrier with leakage from micro aneurysms. Fig. 3(A) and 3(B) shows the images of the two.

III. AUTOMATED DIABETIC MACULAR EDEMA DETECTION

The generic DME detection method using OCT images is illustrated in Fig. 5.For detection of DME using OCT, first of all OCT images of the macular region are taken. Then pre-processing is done to isolate the regions of interest from the rest of the picture is sub retinal layers etc. Then after extracting the thickness profile of the macula, feature extraction begins which refers to the simplifying of image according to certain features and features may vary according to the technique being used. In the end, a hybrid classifier build through a number of training and testing datasets is used to classify the image as DME or Normal.

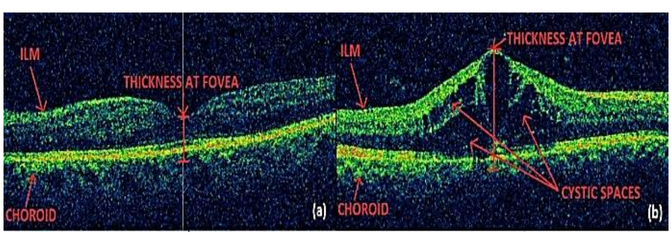

Fig.2.Comparison of Normal and Effected OCT image for Thickness

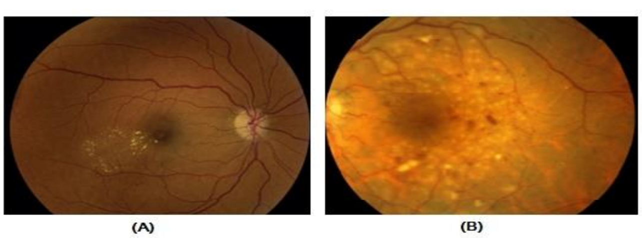

Fig.2. (A) Focal Macular Edema (B) Diffused Macular Edema

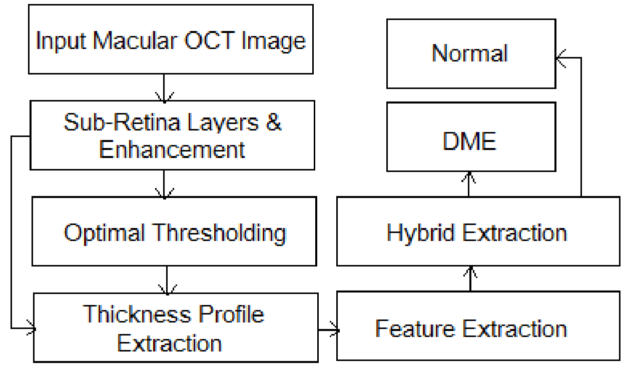

Fig.3. Generic Method for Detection of DME using OCT

IV. OPHTHALMIC IMAGING TECHNOLOGIES

Images play a vital role in the detection and classification of DME. The more clear and noiseless a picture is, the more chances that the results yielded would be accurate. There are many techniques to capture the images of eye including Fundus images, Confocal Scanning laser Tomography (CSLT) and Optical Coherence Tomography (OCT) etc but the one under consideration is OCT. Optical Coherence Tomography, used for the detection and classification of DME, uses light and image is generated on the bases of reflected light capturing the internal details of eye [11]. So far, OCT has proved to be an efficient approach for the detection and classification of DME. One of the benefits of using OCT images is that it’s non-invasive and it detects early stages of macular edema better as compared to other methods. Moreover, OCT images are easier to be classified. A simple method to do so is to extract features based on Local Binary Patterns (LBP) as it has been observed that features extracted from LBP are highly discriminative [2]. Another advantage of using OCT is its quantitative assessment, rather than the qualitative evaluation performed with bio-microscopy or fluorescein angiography [3]. Fig. 6 shows the comparison of OCT and Fundus images and the successful detection in the OCT image.

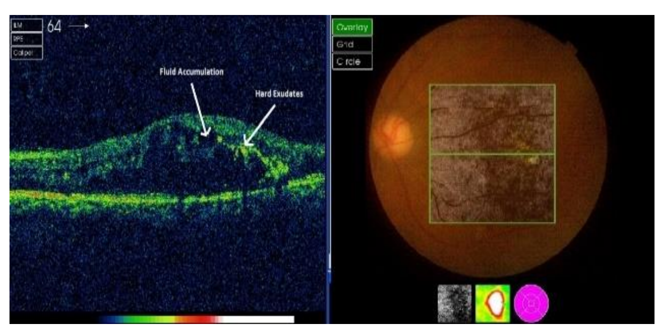

Fig.5. OCT image showing CME and DME clearly and the Fundus image of the same person

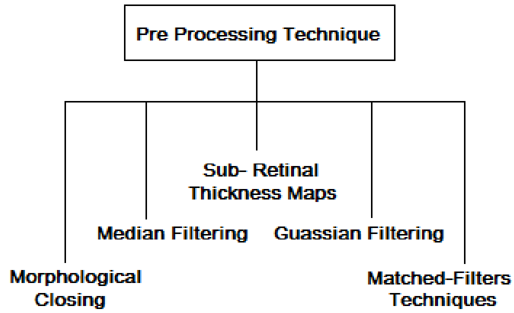

Fig.6. Pre-Processing Techniques used in detection of DME

V. PREPROCESSING TECHNIQUES

Different preprocessing techniques have been used on images to acquire better and accurate results in detecting Diabetic Macular Edema. Fig. 7 shows different techniques used in pre-processing for detection of DME.

Sub-retinal thickness maps for up to 6 retinal layers were segmented and de-noised by using Wiener De-convolution in [1] to compare with manually segmented thickness maps. In [5] preprocessing was done using Gaussian filters for noise removal. For OCT speckle noise, they have used Median filtering in [6] since it smoothens the sub-retinal layers. Figure 6 shows the original and de-noised image after using median filtering. In [7] Matched filter technique is used to determine the location of blood vessels. Morphological closing is used for the detection of exudates in [8] because it smooth's dark regions such as hemorrhages and blood vessels.

VI. FEATUREEXTRACTION TECHNIQUES

Feature extraction is the key process for the accuracy of the whole system. More distinguished and better fabricated features lead to accurate detection of them and a better quality of the system. Different automated feature extraction techniques have been used to obtain better and accurate results while detecting DME and make the system more flawless. In [1], combination of thickness measurements of each image frame in the OCT image stack is used to derive thickness maps and 2-D bi-linear interpolation is used to estimate intermediate thickness between two consecutive image frames.

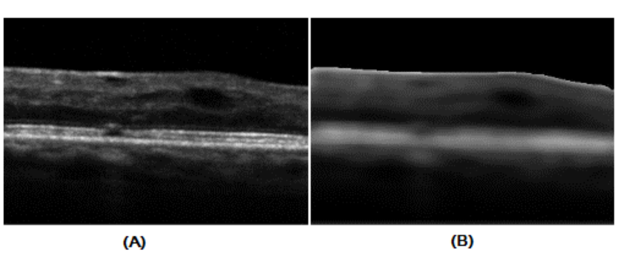

Fig.7. (A) Original Image (B) De-noised Image after Median Filtering

In [5], binary values of PREA, RNFLA and AOB are collected to detect features like bubble or drusen to classify the disease. An automated algorithm detects cyst are in [6] and the Hadamard product of the masks generated from IPR, INR, ONR with image containing True Cyst (TC) regions determines the location of the cyst. [7] Uses empirical linear transformation to get Fluorescein Leakage Maps (FLM) of FFA images to compare with OCT images and derive the correlation coefficient. In [8], different features of exudates like Area, Compactness, Mean Intensity, Mean Hue, Mean Saturation, Mean Value and Mean Gradient Magnitude are derived using different formulae. In [10], features like Mean, Median, Standard Deviation, Entropy and Grey-level co-occurrence matrix (GLCM) features which are contrast, Homogeneity, Energy and Correlation are extracted from the immediate region around macula.

VII. MACHINE LEARNING TECHNIQUES

Many Machine Learning (ML) techniques have been used to detect and classify DME. Table 1 shows different techniques used for the detection and classification of DME. In [5], binary classification using image segmentation to detect drusen or blood bubble is used for the classification of DME and has achieved an accuracy of 87.5%. [1] Uses 3-D localization to detect thickness maps for the detection of DME.

TABLE 1: MACHINE LEARNING TECHNIQUES FOR DETECTION/CLASSIFICATION OF DME

Machine Learning Technique		**DME Detection**	**DME Classification**	**Accuracy**
Binary Classification by image segmentation		No	Yes	87.5%
3-D localization using thickness maps		Yes	No	-
Cysts detection in regions	IPR	Yes	No	88%
	INR			86%
	OPR			80%
Fluorescein Leakage Maps (FLM) using Empirical Linear Transformation		Yes	No	-
Bayesian Classifier		No	Yes	-
Gabor Filter Bank		Yes	No	97.59%
Region Based Method for detection of cases	Most Severe	Yes	No	98%
	Severe			90%
	Moderate			85%
	Normal			80%
Support Vector Machine (SVM)		No	Yes	86%
Texture Features using Segmentation Techniques		Yes	No	-

In [6], algorithm is used for the detection of cysts in inner plexiform region (IPR), inner nuclear region (INR) and outer nuclear regions (ONR) which lead to the detection of DME and thissystem has achieved an accuracy of 88%, 86% and 80% in the respective regions and has a mean error of 4.6%. In [7], empirical linear transformation is used to produce Fluorescein Leakage Maps (FLM) for the detection and quantitative assessment of DME. In [8], Bayesian Classifier using Gaussian functions known as Gaussian Mixture Model (GMM) [8[15]] is used for the classification of DME and Exudates detection using Gabor Filter Bank is used for the detection of DME. The proposed system has achieved an accuracy of 97.59% for the detection of DME [9]. Used region based method to achieve the detection and severity of DME by exudates detection in those regions and has achieved an accuracy of 98%, 90%, 85% and 80% for most severe, severe, moderate and normal cases respectively. In [10], texture features detection around macula is used for the detection of DME and Support Vector Machine (SVM) classifier is used for the classification of DME and the proposed method achieved an accuracy of 86%.

In this method, classification is achieved by using SVM which separates the data in two classes; Normal and Abnormal. It does that by separating the data in the described two classes by picking the best hyper plane having largest margin i.e. the largest distance between nearest points. Eq. 1 shows the distance in this case, between the data points and hyper plane.

$$r = \frac{W^T X + b}{\|W\|} \tag{1}$$

In [6], pseudo code I shows the mathematical process for the detection of cysts in inner plexiform region (IPR), inner nuclear region (INR) and outer nuclear region (ONR).

VIII. DATA SET USED FOR EVALUATION

Data set is the key to determining the accuracy and performance of a system. Data set is used to test and train a system under different scenarios to make it ready to yield results under any circumstances. It means that a data set with higher number of samples would test and train a system better and make it reliable and flawless.

Different data sets having different number of samples have been used to test accuracy of different techniques used for DME detection. In [5], a sample of 16 OCT images were used out of which 10 images were of AMD and 6 of DME and the system was able to classify 87.5% images accurately. In [1], 2 image stacks of 203 images of 10 healthy eyes and 357 images of 15 patients eyes obtained from Heidelberg Spectralis Imaging System at the department of Ophthalmology in University of Minnesota were used and correlation factor turned out to be r> 0.7.

Pseudo Code I: Detection of Cysts represented in Mathematical Model

Require: $G_w \leftarrow mask(NFL, PIS)$
Require: $I_{cyst} \leftarrow \{enhance((1-Y)\circ G_w)\} > 0.7$
Require: $[mean_o, max_o] \leftarrow$ mean and maximum pixel value of the ONR
Let C_i represents all regions in $I_{cyst} \forall i = 1, 2, \ldots\ldots$
Let Small Cysts (SC)= {}, Large Cysts (LC)= {}, Broken Large Cysts (BLC)= {}, $\hat{x} = 0$, True Cysts (TC)= {}
Step 1: $\forall C_i$
if $\frac{major\ axis\ length(C_i)}{minor\ axis\ length(C_i)} < 7$ and $area(C_i) < 2000$ **then**
$SC \leftarrow C_i$
else
$LC \leftarrow C_i$
end if
Step 2: $\forall SC(j)$
D(j) $\leftarrow$ cyst decision$(SC(j), mean_o, max_o)$
if D(j)=1 **then**
TC $\leftarrow$ SC(j)
$\hat{x} = \hat{x} + area(SC(j))$
end if
Step 3: $\forall LC(k)$
$BLC(l) \leftarrow \{enhance((1-Y)\circ LC(k))\} > 0.8$
Step 4: $\forall BLC(l)$
$D(l) \leftarrow$ cyst decision$(BLC(l), mean_o, max_o)$
if D(l)=1 **then**
TC $\leftarrow BLC(l)$
$\hat{x} = \hat{x} + area(BLC(l))$
end if
return $\hat{x}$, TC

In [2], 2 data sets; Singapore Eye Research Institute (SERI) having 16 DME and 16 Normal images and DUKE with 15 AMD, 15 DME and 15 Normal images were used. In [6], 120 OCT images of 25 DME patients were used which yielded an accuracy of 88%, 86% and 80% for IPR, INR and ONR regions with the correlation of 90% between estimated cystoid are and manually marked area and a mean error of 4.6%. In [7], 13 Fluorescein image sequences for 13 patients were used and the system showed varying correlation. In [8], 3 databases; STARE, DiaretDB0 and DiaretDB1 were used and the system achieved an accuracy of 97.59% for detection. In [9], a dataset of 100 images of MESSIDOR was used for testing and the system achieved accuracy of 98%, 90%, 85% and 80% for most severe, severe, moderate and normal cases respectively. In [10], 60 images (45 for training and 15 for testing) were used and the system achieved 86% accuracy.

IX. CONCLUSION

Diabetic Macular Edema (DME) is the main cause of vision loss in Diabetic patients and does serious damage to the eyesight. In spite of being a serious disease, its symptoms are nearly unnoticeable and develop over a time period until they're late enough to be dealt with and treating it becomes impossible. So far, many automated techniques have been developed and used to detect it in its early stages so that loss of sight can be prevented in patients. However, Machine Learning (ML) techniques using OCT have proved to be more successful than others in yielding accuracy of 80 to 90 and above percent.

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