A Review on Fundus Imaging

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Abstract: In this paper a history of fundus imaging is presented followed by an overview of different diseases that can be diagnosed by image analysis of fundus images. The need of preprocessing and some pre-processing approach for fundus images have also been discussed. A brief literature review as also been done of the approaches employed to detect two prevalent ailment- glaucoma and diabetic retinopathy.

Keywords: Fundus imaging, image preprocessing, glaucoma, diabetic retinopathy, non invasive.

Introduction

Biomedical imaging has emerged as an impressive tool in the repertoire of medical practitioners enabling non-invasive diagnosis of wide variety of diseases. Although, the origins of medical imaging can be traced back to the discovery of X-ray in 1895 by W.C. Rontgen. However the field has gradually progressed and a present not only radiations from entire breath of the electromagnetic spectrum(Gamma –PET,CAT) to radio-MRI, MRI but also other imaging modalities are used for imaging like ultrasound and electron-microscopy. Moreover multimodal imaging which utilized combination of multiple imaging modalities is also developing into effective mechanism for diseases diagnoses.

Like other organs, medical imaging techniques have been employed for detecting different diseases of eyes and it has been found that majority of the eye diseases can be detected using retinal imaging (also known as Fundus image). Additionally retinal imaging also helps in diagnoses of other diseases like diabetes, hyper tension etc. Early diagnosis of eye diseases is imperative otherwise it may lead to total loss of vision. This paper presents a bird's eye view of eye diseases and their diagnosis using fundus imaging. The rest of the paper includes description of fundus images, its history and its relation to different eye and other diseases.

Human eye is a three layered structure with cornea and sclera forming the outer cover, Choroid in middle and inner most retina (sensor screen) having rods and cones on its surfaces. Fundus image is the image of retina of the eye. The main component of fundus images are shown in "Fig 1". The point where blood vessels intersect and leave the eye is known as optic disc or optic head. As it devoid of photoreceptors so this point is also known as blind spot. Macula is a oval shape, yellow pigmented area at the center of retina Fovea is a point in macula where maximum number of cones are concentrated. Cones are consider to be responsible for photopic (shape vision) whereas rods take care of scotopic vision (dark light vision).

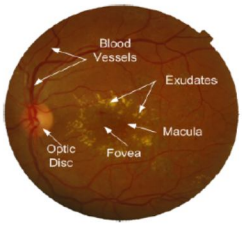

Figure1. Fundus image with its component

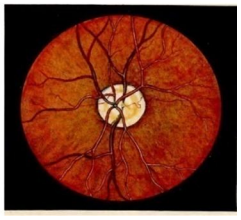

Figure2. First retinal image

History of fundus imaging

Eye due to its inherent characteristics, disallows direct inspection of itself because when light is passed through pupil retina makes it appear red. So some special technique was needed for imaging the retina. The French physician Jean Mery was first one who got image of retina of cat. He showed that if a live cat is immersed in water, its retinal vessel is visible from outside (not practical in case of humans). This led to the invention of the principle of ophthalmoscope in 1823 by Czech scientist Jan Evangelista Purkinje and its reinvention by Charles Baggage in 1845, who also introduced the concept of programmable computer, he also developed link between computation and retinal images. Von Helmholyz in 1851 [1] provided another modification technique for capturing retinal images. The first image of retina was published by a Dutch ophthalmologist Van Trigt in 1853(Fig2). The first ever fundus camera was invented in 1910 by Gullstrant and the concept still used. He received

Nobel Prize for this invention. The major limitation for fundus camera was that it obtains 2D images of 3D semi-transparent retinal tissues. The first approach for getting 3D shape was stereo fundus photography, where multiple images were taken from various angle and then recombine to give 3D images (described by Allen in 1964), which led to development of confocal scanning laser ophthalmoscope where multiple images were taken at various depth. Its drawback was that the depth resolution was approximately 100 micrometer; whereas the depth of the whole eye is 300 to 500 micrometer. With the development of super luminescent diodes, femtosecond laser and the application of optical coherence tomography (OCT), 3D imaging of eye has become possible.

Different agencies has collected database of image pertaining to various eye diseases. The most popular databases reported and used by researchers in literature have been listed in "Table 1" [9, 20, 21].

Diseases

The branch of medical science which deals with the study and treatment of diseases in eye are known as ophthalmology. Image processing tools can be used to diagnose many eye diseases. Some of them are listed below :-

- *Diabetic retinopathy (DR)*: It occurs due to diabetes. Diabetes is the fastest growing diseases in world. According to survey in 2000 by WHO, India ranks 1st (31.7%), China at 2nd and USA at 3rd. It's expected to double till 2030 from 171 million to 366 million, with maximum increase in India of 79.4 million. About one third of people suffering from diabetes, suffer from diabetic retinopathy. It can be prevented through early diagnosis. It can be diagnosed by finding exudates in fundus images.
- *Macula edema*: It's most commonly known as type 2 diabetes which is the primary cause of blindness with diabetes. It's caused due to breakdown of blood retinal barrier which leads to damages of photoreceptors. It causes thickening of retina. It can be diagnosed by detecting hard exudates in eyes.
- *Glaucoma*: According to vision 2020 India.org, glaucoma is the third cause of blindness in India. It's characterized by gradual damage to the optic nerve. The hallmark of glaucoma is cupping of optic disc and it can be diagnosed by calculating cup to disc ratio.
- *Age related macula degeneration (AMD):* Generally occurs due to ageing (>40 year).It's of two type, dry and wet macular degeneration (cause of dry macular degeneration is not known). Dry (exudative) degeneration occurs when abnormal blood vessels start growing in underneath retina; these blood vessels may leak fluids causes blurring central vision. So it can be diagnosed by seeing blood vessels extraction and exudates detection from fundus images.
- *Hypertension*: Hypertension has been related by WHO as one of the most important cause of death worldwide. This occurs due to high glucose level and high blood pressure. It can be diagnosed by calculating change in ratio of the diameter of retinal arteries and veins, known as A/V ratio. If this ratio decreases, it show increase in risk i.e. widening of veins and thinning of arteries.

Figure3 a. Normal eye Figure3 b.Glaucoma eye Figure3 c.DR eye Figure3 d. AMD

Table1: Database used in eye

Name of database	**Number of images**	**sources**
Messidor (Method to evaluate segmentation and indexing techniques in the field of retinal ophtalmology)	1200 fundus image (divided in three set, each has 4 subset). Contain healthy, diabetic retinopathy infected and macula edema infected eyes.	www.adcis.net/en/Download-Third-party/Messidor.html
Image science institute: drives (Digital retinal images for vessel extraction)	40 fundus images ,33 healthy eye, 7 mild diabetic retinopathy	www.isi.uu.nl/Research/Databases/DRIVE
DIARETDB1-Standard Diabetic retinopathy Database calibration level 1	89 fundus images, 84 diabetic retinopathy,5 normal image.	www.it.lut.fi/project/imageret/diaretdb1/index.html
DIARETDB0-Standard Diabetic retinopathy Database calibration level 0	130 fundus images, 20 normal and 110 diabetic retinopathy infected.	www.it.lut.fi/project/imageret/diaretdb0/index.html
High-Resolution fundus (HRF) image database	15 healthy eye 15 glaucoma eye 15diabetic retinopathy infected	www5.cs.fu.de/research/data/fundus-images/

Challenges in fundus imaging

For accurate detection and diagnosis of diseases, good qualities of fundus images are required and studies Ref [1] have shown that 12% of captured fundus images cannot be analyzed. Some of the challenges encountered in eye disease diagnosis.

- There is a possibility of non-uniform illumination and poor contrast due to 3D concave shape of eye.
- Geometry of sensor array.
- Involuntary eye movement during image acquisition.
- If different images are taken by different fundus camera then there will be different in brightness. So, before moving towards diagnosis process, brightness of all image need to be made same.
- Sensor noise and other type of noise may be introduced in the image during acquisition.

The quality check of acquired image is based on the distinguishability of blood vessels from background. To check how accurate classifier is we calculate sensitivity and specificity. An algorithm is best if its sensitivity and specificity are high. It can be calculated as

$$sensitivity = \frac{T_p}{T_p + F_N} \quad (1)$$

$$specificity = \frac{T_N}{T_N + F_P} \quad (2)$$

Where, T_p=Number of abnormal image found to be abnormal. T_N=Number of normal fundus image found to be normal. F_N= Number of abnormal fundus image found to be normal(false negative). Fp= Number of normal fundus image found to be abnormal (false positive).

Methodology

Being a Pattern recognition problem, diagnosis of any disease related to eyes using image analysis involves three main step. (Figure 4)

- Pre-processing.
- Feature extraction.
- Classification.

Preprocessing

Pre-processing is the first step in any image analysis technique and facilitates the features extraction process. A brief review of few pre-processing technique used by researcher is given

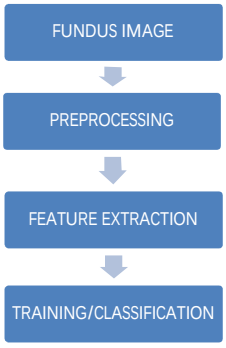

Figure4. A general pattern recognition block diagram

Illumination equalization:

Non-uniform illumination can be overcome by removing mean intensity from fixed size windows used the following expression [2, 3].

$$I_{eq}(r,c) = I(r,c) + m - \hat{I}(r,c) \quad (3)$$

where, m=average intensity and $\hat{I}$(r,c)=mean intensity value of each pixel within window nxn. The size of window can be varied. In [2] window size varies between 30 and 50. Where as in [3] the window size kept fixed (40x40) the resulted image look similar but ROI (region of interest) is decreased by 5 pixels. Some authors have applied illumination equalization on a specific color channel; in ref [4] illumination equalization is applied on green channel.

Color normalization:
The information of color has a potential for classification of lesion in retinal image. But due to imaging devices and lightning geometry, pixel value of fundus image may alter. This results in ineffective classification. Few color normalization techniques employed are:

- *Gray-world normalization*: This process aim to eliminate the effect due to color illumination [5, 6]. It follow following equation

$$r^{new} = \frac{r}{R_{avg}}, g^{new} = \frac{g}{G_{new}}, and\ b^{new} = \frac{b}{B_{new}} \quad (4)$$

  where $R_{avg,}$,G_{avg},B_{avg} is the mean value of all the pixel in R,G and B channels .
- *Comprehensive normalization*: In this process chromaticity (quality of color, independent of brightness) normalization is done and the normalized values are defined as [7]:

$$r = \frac{R}{R+G+B}, b = \frac{B}{R+G+B}, and\ g = \frac{G}{R+G+B} \quad (5)$$

Only two chromaticity value need to be computed since r+g+b=1. Chromaticity is the representation of digital image which can be affected due to invariant light geometry. Practically both light geometry variation and color illumination variation do not occur separately. So first, comprehensive normalization is performed, followed by grey-world normalization.

Histogram equalization: In this method, RGB image is separated into individual R,G,B channel. Then each channel individually equalized by histogram equalization technique [7]. This method will increase the influence of blue color in image.

Histogram specification: This technique is applied when some image is to be generated with certain histogram. In this, the RGB image is treated with histogram equalization and then with histogram matching [7], where reference image is original fundus image.

Feature extraction

The images obtained usually contain a great deal of irrelevant background detail. So, during feature extraction this unwanted component is removed and finally characteristics pertaining to particular diseases are extracted. Feature extraction approaches for diabetic retinopathy and glaucoma are given below.

Diabetic retinopathy

For detection of diabetic retinopathy Preprocessing followed by optical disc removal is carried out since the color of optic disc and exudates is same. In this case abnormalities in retinopathy eye include microaneuryms (small red dot shown by arrow) hemorrhages, hard exudates, neovascularisation. These are depicted in "Figure4".

Detection of exudates :In ref[9], authors used median filter for removing noise, segmented lesion (bright and dark) pixel by thresholding and then exudates regions where identified using Bayesian and k-nearest neighbor classifier. Bezdek, Keller, Krisnapuram, & Pal used color normalization for preprocessing and fuzzy c-mean cluster and neural network for exudates extraction [10]. "Fig5" show general steps for exudates segmentation.

In ref [11] Nath, M. K & Dandapat, uses independent component analysis (ICA) on sub-band of wavelets for detection of changes in fundus images. The Steps followed are splitting of color components, pre-processing, wavelet decomposition, sub-band selection then formation of matrix for ICA. In ref [12] Narasimhan, Neha& Vijayarekha, they first localized optic disc then preprocessed the image by color equalization, for segmentation edge detection technique was used to detect edge from smooth image, color histogram thresholding is used for exudates detection. In ref [13], Hassan, Tahir, Yassin, Yahaya & Shafie, they proposed technique called radar chart and Color Auto Correlogram (CAC) technique. In that paper, performed histogram equalization on individual channel of image for preprocessing, eliminate optical disc manually, and then extract exudates and non-exudates color using neural network. The radar chart was used for comparing eye having exudates and eye without exudates

Detection of neovascularization: Neovascularization is growing of new blood vessels in eyes, which is indication of proliferative diabetic retinopathy. For detection of new vessels, blood vessels are extracted. In ref [14] Antoine, Carrette, Murenzi & Piette have uses 2D Gabor wavelet approach for vessel extraction . Hoover, Kouznetsova & Goldbaum, used matched filter approach. However matched filter approach has a disadvantage that it not only enhances blood vessels but also brighten the part of image. Therefore 2D Gabor filter is better in comparison as it provides the facility of direction selection and fine tuning at specified frequency. An iterative method is per formed, suggested in ref [15] threshold value is decreased in order to eliminate falls edges. A window of 15x15 size applied over blood vessels for detecting abnormal vessels.

Detection of microaneurysm and hemorrhages: Both these abnormalities are red in color so according to some authors, they prefer to remove blood vessels before feature extraction. In ref [12] Narasimhan, Neha & Vijayarekha morphological top-hat transformation approach is used, in which original image was subtracted from opened image (i.e. morphological open operated image). This method can be performed linearly as well as rotationally. In rotational method, the structural element is rotated in 12 different orientations in order to get the best result. In ref[9] authors introduced a 'moat operator' for detecting features of NPDR automatically using information from green color channel.

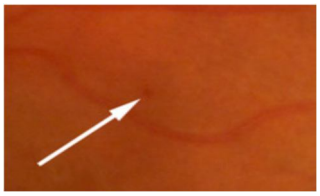

Figure4a. Microaneuryms

Figure4b. Hemorrhages

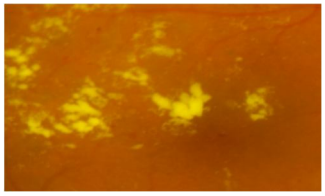

Figure4c. Exudates

Figure4d. Neovascularisation

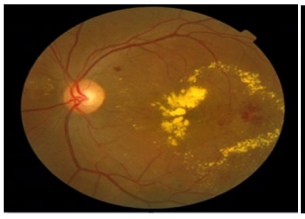

Figure5a. Fundus image

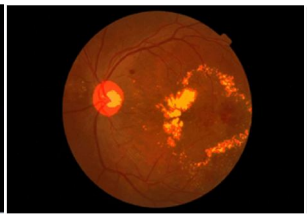

Figure 5b. Pre-processed image

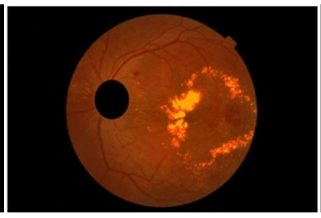

Figure 5c.Optical disc remove.

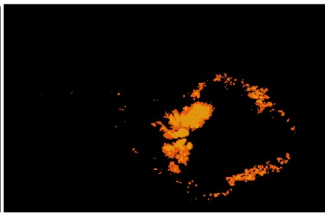

Figure5d.Exudates extraction

Glaucoma

Glaucoma is a disease which can be diagnosed beforehand by keeping look on optical nerve head (OND) or optical disc. The optic disc is a point from where signal of eyes is transferred to brain. It appears bright in fundus image and circular in shape. It is the one particular area which is devoid of receptors.

The preprocessing for glaucoma detection includes blood vessels (dark pixel in fundus image) and exudates (brightest part of fundus images) because these act as a destructor in diagnosis process. As blood vessel are intersected at optical disc region which will cause problem while extracting optic cup, Exudates and optical disc are the brightest part of image so it will also provide disturbance in process. Ahmad, Yamin, Shakeel, Gillani & Ansari [16] converted RGB image into grayscale image and carried out morphological reconstruction after morphological opening and closing of image. Opening suppresses bright part of image and closing suppresses dark part of image. The region where pixel values were found to be less than 30 pixels were treated as non-vessels. In ref[8] Youssif used simple edge fitting algorithm to segment the blood vessels and maximized similarity between predefined 2D Gaussian template and the fundus image.

Abnormality in glaucoma eyes can be extracted in two ways first is structural feature and other is texture feature extraction. The way of finding that patient is having glaucoma or not is by using CDR (cup to disc ratio) i.e. by structural feature extraction, shown in "fig6". The difference between optic disc and optic cup is that of both optic cup is brighter then optic disc, which can be seen easily in green channel. Optical cup extraction is challenging task since it's embedded inside optical disc. Different approaches have been employed to extract CDR. In ref [17] Agarwal and et al the region of interest cropped (optical disc) manually (200x250 approx). Since optic cup is the brightest part so they converted image into binary form to get optical cup. For optical disc, they converted the RGB image into HSV image; V plane is extracted and converted into binary image. Then compute area of both disc and cup to calculate CDR. If CDR is found more than 0.5 then the patient is considered to be having glaucoma. "Fig7" shows general steps for feature extraction (CTR).

Similarly like CDR, NRR (Neuroretinal rim) which is area between optic disc and optic cup can also be calculated. This can be calculated by just applying AND operation on obtained optical disc and optical cup.

Some researcher's used segmentation technique for finding CDR. Centre of optic disc and optic cup are estimated, followed by thresholding for segmentation. The threshold value is calculated by averaging the value of a grey level pixel. In ref [19] k mean cluster operation is used (keeping k=2) in preprocessed ROI(region of interest). K mean cluster method is unsupervised iterative method .which divides image into k number of cluster. It is the fast and effective method for color segmentation. For better segmentation, the RGB image is converted into LAB (L is for lightness, a and b is for color opponents green-red and blue-yellow) color space. Performance function of k mean is given by

$$J_{km} = \sum_{j=1}^{N} min_{j=1}^{k} ||x_i - m_j||^2 \quad (6)$$

The image obtained after k mean, Canny edge detection algorithm used for edge detection of both optic disc and optic cup. Canny edge detection has an advantage that it also removes noise. Then elliptical fitting method is used for smoothing the boundary. It works on least square fitting algorithm. Finally, CDR is calculated.

In ref [17] Agarwal and et al used adaptive threshold method for segmenting disc and cup part. For that they take green channel of the image and then they find mean and standard deviation of it as a feature. They calculated threshold value by equation as

$$T_{disc} = 1.2\, Xsum(mean, standard\ deviation) \quad (7)$$

Cup is brighter than disc and its threshold value is calculated by

$$T_{cup} = 1.25\, X\, (T_{disc}) + diff(mean, median) \quad (8)$$

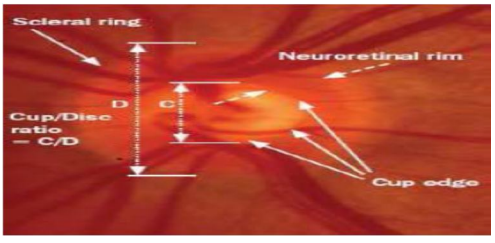

Figure6. Cup and disc in fundus image

Figure 7a. Region of interest

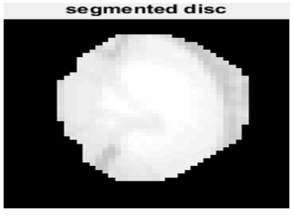

Figure 7b. segmented disc

Figure 7c. segmented disc

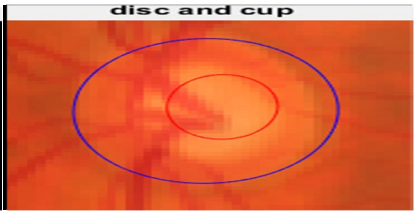

Figure 7d. cup to disc ratio calculation

The values above threshold are kept 1 and remaining 0. They found that if CDR is more than 0.3 then patient is having glaucoma.

The texture-based approach can also be used but are not preferred since accuracy is less as compared to structural based approach. Some of the texture changes in glaucoma eye are listed in Ref [18]. These include: (i) mean grey level, as in glaucoma eye cup widen therefore mean grey level of optic disc is greater than mean grey level of optic disc in normal eye, (ii) superpixel which is defined as the pixel value larger than or equal to threshold value T=0.9 in the red channel. Since glaucoma eye will have more number of superpixel value in optic disc than normal eye, due to enlargement of optic disc in glaucoma eye.

For improving accuracy in detection, some of the researchers have proposed hybrid approaches. In ref [18] Shehryar, Akram, Khalid & Jameel used the result obtained from three-technique (a) circular Hough transform followed by active contour, second technique used (b)super pixel based feature extraction and classification and (c) was ellipse fitting. Best result obtained was used for further processing.

Conclusions

In this paper a review of eye diseases and their diagnosis uses retinal images is presented. The progress made in this area builds confidence that in near future hand-devices can be developed which can be utilized by ophthalmologist and patients alike for disease diagnosis.

We expect development in following areas

- Cost efficient system: - By cost efficient we mean to make small portable smart camera which is cost efficient for imaging. As well as the camera must be the high-resolution camera
- Patient friendly: - system developed must be friendly to use. So that he can easily do his checkup.

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