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REVIEW OF OPTICAL COHERENCE TOMOGRAPHY IMAGE ANALYSIS FOR RETINAL DISORDERS

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Abstract

Though glaucoma is the second leading cause of blindness all around the world, it is also caused due to various disorders like Cystoid macular edema (CME), and Symptomatic exudates-associated derangements (SEAD). These are caused due to excessive accumulation of fluids within the retinal layers. Hence automations in diagnosis of fluid volume plays a key role I the treatment of such disorders. Optical Coherence Tomography (OCT) measures the optical reflections of the internal structures of the biological tissues. It also serves a major tool in diagnosing several blinding diseases including Age related macular degeneration (AMD), retinopathy, glaucoma, and Cystoid Macular Edema (CME). This paper reviews various methodologies proposed so far in terms of their sensitivity, specificity, precision, accuracy and shortcomings. It also proposes some techniques to overcome the shortcomings of these methodologies.

Keywords: Glaucoma, Optical Coherence Tomography, fluid pressure, vision loss**.**

Introduction

Spectral Domain Optical Coherence Tomography (SD-OCT) is recently developing Imaging Technique [1], which clearly identifies numerous diseases in various layers of the retina[2]. Retina is the interior layer of eyes which converts the incident light signals into neural signals, which are transmitted to the brain. Retina consists of various pigments of rods and cones, which are responsible for dimlight and color visions respectively. Retina has several layers of pathological and physiological importance. Any damages in these layers lead to several high risk abnormalities including vision loss. OCT remains a vital tool to diagnose several blinding diseases including Age related macular degeneration (AMD), retinopathy, glaucoma, and Cystoid Macular Edema (CME). Fig 1 shows an OCT device.

Fig-1: Optical Coherence Tomography Image Acquisition Device.

Earlier works in the analysis of OCT Images focused on segmentation of Intraretinal layers [3]-[12] but segmentation of fluid filled regions, [13][14] and optical disc is also much essential. The advantage of using an OCT Image instead of Fundus photographs is that these present a three dimensional view of the retinal layers. High sensitive micron scale resolution images could be obtained using SD-OCT by low coherence interferometry technique. OCT and B mode ultrasound are almost similar except that low coherent source is being used. Optical Reflections of the internal structures of the biological tissues are measured cross sectionally in the procedure of OCT [15]. Different information on the time of flight delay is obtained from the coherence property of the reflected light. This delay information could consequently be used in determination of the longitudinal location of the reflection sites. Multiple longitudinal scans are performed by the OCT Systems, at a series of lateral locations, thereby providing a two dimensional mapping of the reflection sites in the sample. The rate of data acquisition is increased by continuous motion longitudinal scanning thereby making the two dimensional imaging a possibility. Unlike X Ray Computed Tomography or Magnetic Resonance Imaging, very lesser mathematical computations are implemented in reconstruction of OCT Images. Measurement of the intraocular pressure quite often fails to predict the progression of glaucoma [16]. Various abnormalities like loss of visual field and cupping of Optical Nerve Head (ONH) could be clinically diagnosed only after 50% of Nerve fiber loss [17]. Due to the cylindrical nature of the nerve fibers, the incident angle of light determines the strength of the backscattered signal from Retinal Nerve Fiber Layer (RNFL) [18]. This accounts for the RNFL Signal attenuation, which is observed at the margin of the optic disc, where the nerve fibers descend into optic nerve [15].

It could be understood that various images of clinical significance could be obtained using this modality of imaging. OCT serves a useful modality to analyze retinal images qualitatively as well as quantitatively. The need of these automated analysis are increasing as the diseases identified lead to blindness consequently. The extent of disorder in turn plays a significant role in deciding the dosage of drug to be injected. Accurate medication dosages should be kept up in order to avoid complications from over treatment.

The performance of the various systems proposed could be tested in terms of sensitivity and specificity. The proportions of correctly identified actual positives are given by the sensitivity whereas the proportions of negatives which are correctly identified are given in terms of specificity. Mathematically Sensitivity and Specificity serves a tool to measure accuracy which could be given by,

$$Sensitivity = \Sigma\ True\ positive\ /\ \Sigma\ Condition\ positive \quad (1.1)$$

$$Specificity = \Sigma\ True\ negative\ /\ \Sigma\ Condition\ negative \quad (1.2)$$

where, the term 'True positive' refers to the correctly identified samples, False positive indicates the incorrectly identified ones, 'True negative' denotes the correctly rejected samples and false negative represents the incorrectly rejected ones.

In turn, precision and accuracy could be defined in terms of true and false positives, true and false negatives as follows:

$$Precision = \Sigma\ True\ positive\ /\ \Sigma\ Test\ outcome\ positive \quad (1.3)$$

$$Accuracy = (\Sigma\ True\ positive + \Sigma\ True\ negative)\ /\ \Sigma\ Total\ population \quad (1.4)$$

The degree of closeness of measurements of a quantity to that actual value is referred to accuracy. The degree to which the repeated measurements under same conditions remain identical is given by precision. It could be understood that it is in turn an essentiality to measure these statistical parameters for any system in order to quantify its efficiency and performance.

An effort has been put to highlight the existing methodologies and brief review of the recent publications has been carried out in this paper. This paper has been prepared in such a way that section 2 deals with the related works. Also a methodology has been proposed in section 3, while, and section 4 ends with a conclusive statement on the presented review.

Related Works

Delia Cabrera Fernandez et al., demonstrated the cystoids and subretinal fluid spaces in the OCT Images [13]. As the images are more prone to speckle noises, which are multiplicative in nature, the use of filters for their suppression was extensively discussed. Two different techniques, namely, gaussian filtering and anisotropic diffusion filtering were evaluated. Focusses were made on to preserve the edges during the process of noise removal. In other words, ideas were framed not to lose any edge informations, assuming to improve the quality by reducing the speckle noises. The anisotropic diffusion filter proposed by Perona and Malik [19], which was based on multiscale edge detection scheme was used and found to be more efficient when compared to the Gaussian filtering. The performance of the edge preservation was then qualitatively analyzed by a correlation parameter, χ which was expected to be close to unity for optimal effect of edge preservation.

Not limiting to the noise removal, also the lesions were isolated, for which, the quantitative analysis of the surface area and the volume were performed. The isolation was basically with the Snake algorithm. A Gradient Vector Flow (GVF) based snake was used in conjunction with the preprocessed OCT images in order to obtain accurate shape description of the regions filled with fluid, associated with AMD. The optimum parameter values of the GVF Snake contour fitting the lesion boundary in the images were found [13]. Performance of the snake model for peripheral, central and multiple regions with fluid in the OCT images were evaluated.

As preprocessing plays significant role in the proposed model (due to presence of speckle noises), the proposed noise filtering system supports for accurate convergence of the snake to the lesion boundary. The snake initialization procedure was manual, as the snakes were designed to be interactive. Some automated snake initialization methods, which can also detect multiple fluid filled regions, could be identified. The system success entirely depends on where the snake is initialized and how the snake is being guided.

Not exploring all the Macular disorders, *Gwenole Quellec et al.,* aimed at determining the footprints of fluid filled regions, called Symptomatic Exudate Associated Derangements (SEADs). The automated SEAD detection method was validated with an interactive segmentation approach. The methodology proposed was easily understandable, yet a complex approach, as it involves three dimensional analyses of the images. The steps specified in the system include intraretinal layer segmentation, extraction of various textural features of the segmented layers, classification using the extracted features by means of a k-NN Classifier, to determine if the layer is fluid filled or not. From this data, binary SEAD footprint images were obtained using a probability map followed by thresholding technique. Preprocessing techniques used were wavelet filtering of the speckle noises. In addition to existing techniques of Intraretinal layer segmentation [11], a fast multi-scale 3D graph search method was introduced [14], to detect three additional retinal surfaces from 3D OCT scans centered at Optic Nerve Head (ONH). In turn, totally ten Intraretinal layers were automatically segmented by using multi-scale three dimensional graph search technique [20].

Flattening of the macula in original SD-OCT image was done by using last retinal surface as a reference plane, after which the three dimensional textural feature extractions were done. 21 statistical features were calculated in the flattened layer subvolumes [14]. Various features include the mean, variance, skewness, kurtosis, graylevel entropy, shortrun emphasis, longrun emphasis, graylevel nonuniformity, runlength non uniformity, run percentage, angular second moment, correlation, contrast, entropy, inertia and inverse different moment. In order to reduce the cardinality of textural characterization, these feature values were averaged to form 21 scalar features.

In addition to the above extracted features, the average and the standard deviation of the layer thickness were also computed, numbering to 23 features in total. These features were obtained for several normal retinal surfaces and a threshold value was identified. This deviation threshold was used to classify the retinal layer, whether it is normal or fluid filled. In total, 91 macula centered 3D OCT volumes were obtained from 13 normal and 26 pathologic eyes. The segmentation process was then assessed by experts. SEAD footprint detection under various circumstances are analysed in detail. Since SEADs can appear anywhere within, between, or under these layers, their footprints were detected by classifying vertical, cross-layer and macular columns. This interactive method was tedious and time consuming when compared to the techniques existed. Though this system suggested that evaluation using textural features served a good method even in presence of speckle noises, it lacks identifying the volume of the SEADs identified.

A system was proposed by *Xinjian Chen et al.,* for automated segmentation of SEAD Volumes of AMD Patients. The system was divided into two parts, namely, retinal layer segmentation, and a probability constrained combined graph search graph cut method that refines SEAD by integrating volumes into the graph cost functions as probability constraints [21]. Though the segmentation of SEADs remain a tough task due to low SNR and Shape Variability, the system proposed an automated volume segmentation in three dimensional OCT Images. Previous studies included only semi-automated methods which involved manual initialization [21] in two dimensional images. Authors also proposed a similar SEAD footprint detection in their previous works [14], which remained a two dimensional analysis. An automated segmentation tool was proposed in [22] but it failed to segment upto 30% of the analysed scans. In short, the work aimed at combining the Graph Search (GS) and Graph Cut (GC) methods for segmentation. A surface region graph based approach [23] was proposed to segment multiple regions and multiple surfaces simultaneously. Initialisation included layer segmentation, fitting a surface to bottom layer, and determination of the SEAD Volumes.

Eleven Layer Segmentation of the retina was initially performed [11]. In order to initialize the process segmentation, the voxels with fluid collected were first identified. Various textural, structural, and positional features of the voxels were then calculated, based on which voxel classification was done. In turn a binary image is obtained by using the positive and negative voxels in the dataset [24]. The classification was based on the previously studied k-NN Classifiers [25]. After the training phase, the segmentation was tested with unknown sample [26]. Gaussian distribution was observed in the distribution of the intensity. A post processing method as performed seems to be quite essential [21]. The layers above and below the SEAD were set as the target, so that GS and GC were combined to segment the SEADs. Surface, region and Interaction Cost functions were in the problem of segmentation for the purpose of optimization. The subgraphs were constructed in relation with the previous works [27]. The validation process seem to be effective wherein the segmented outputs were cross verified by the manual segmentation done by retinal specialist using the software described in [28]. The statistical relativity of the manual and automated segmentation was done using linear regression analysis [29], and Bland-Altmann plots [30]. Though the system seems to be reliable and fully automated, the performance relies on the results of initialization. If the probability Constraints were not true, then the entire result proved a failure. Segmentation for challenging dataset (with AMD) were carried out and validated to show its appreciable results on performance.

A fully automated retinal cyst segmentation of images with Cystoid Macular Edema (CME) was proposed by *Gray.R.Wilkins et al.,* [31]. Measurements of the macular thickness can be more error prone in presence of subretinal fluid [32] [33]. As suggested in [34], total cyst volume was estimated which could in turn be used as a metric for identifying CME. Among the various techniques employed in previous works of speckle noise reduction, like anisotropic diffusion filter [10][35][36], spatially adaptive wavelet filter [37], Bayesian least square estimation [38] and bilinear with median filtering [39], the latter was employed. The system was designed to identify the regions of cystoid fluids within the 3D stack, by elimination of the False Positive (FP) from the Region of Interest. The steps included may be summarized as graylevel conversion, noise removal and retinal layer segmentation, SNR Balancing, bilateral filtering, thresholding, tracing of the boundaries, and FP rejection. The design was so simple and user friendly that it executed a single function whose only input was the stack image obtained from the OCT Equipment. It could be seen that various inbuilt MATLAB functions were used for the above specified steps.

The evaluations of the results were done under supervision of experts by means of GUI in MATLAB, which the system easier to operate. With sensitivity and specificity of 91% and 96% respectively, though the system required lesser time for computation, often the blood vessels are also rejected during the process of FP rejection. It could be understood that the preprocessing could have been much more efficient in noise removal. Also the system could have been tested with a wider database. The ability of the system to differentiate the cyst and Intraretinal layers was not evaluated which could have been taken into consideration.

Proposed Methodology: From the literature it could be seen that numerous research problems are still prevalent in this area of research. In Most of the systems initialization played a key role in determining the overall system performance. Also tediousness, lack of user friendliness, and increased time of computation remained a challenge in the literatures reviewed. Not restricting to specific disorder, a system could be developed for the identification of a wider range of retinal abnormalities (including CME, SEAD/AMD). The research objectives chosen from the review of literature are as listed below:

- To develop a User friendly system to analyze wider range of Fluid related abnormalities (including CME, Macular Degenerations/ Edema, SEAD).
- To evaluate the performance of various techniques used for Speckle noise reduction.
- To optimize the features required for classification in terms of time of computation and performance.
- To validate the performance of various classifiers for the specified application.
- To design an Automated Expert system to comment on the input image along with classification.
- To segment the Fluid filled area and present the same with the percentage of Abnormality.

The overall experimental set up of the proposed system is schematically represented in fig.2.

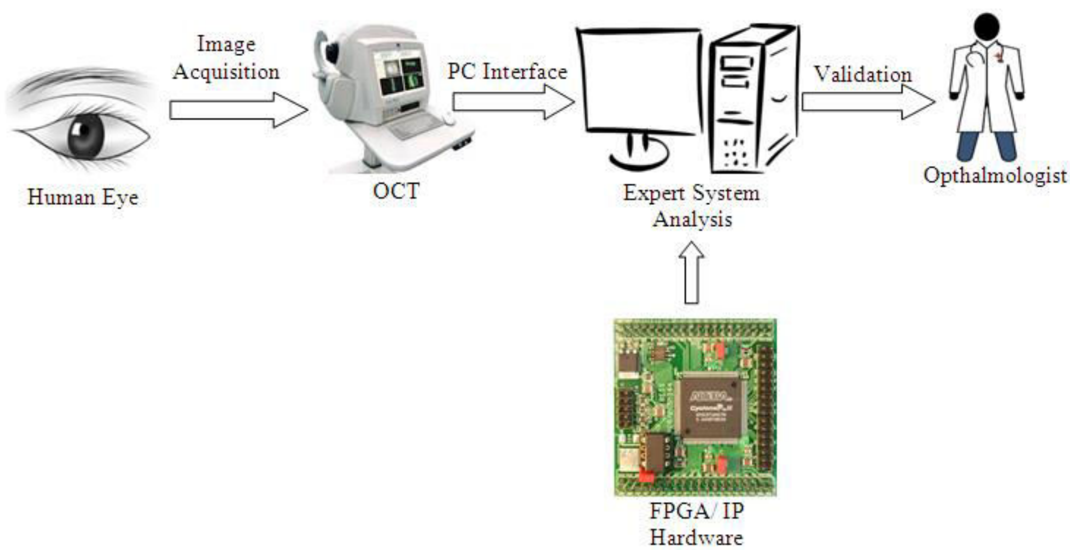

Fig-2: Experimental Setup.

The image of the human eye is accquired by means of OCT Device which is further interfaced with the PC. The OCT Image could be seen in the PC during the time of data acquisition. The data loaded in the PC is then fed as input to the Expert System and is subjected to further Analysis. The analysis is done by specialised hardware like FPGA for fast analysis of data. It is to be remembered that the two dimensional image data should be converetd into one dimensional data before being fed into the Processor. FPGA could be programmed using a PC interface. This analysed data is cross validated by an ophthalmologist in order to evaluate the system performance. Usage of FPGA Kit will enable realtime processing of input images, with improvised speed of processing. Performance, cost, reliability, speed of processing (due to parallel operations) have made use of FPGA an efficient tool for medical image analysis. A methodology is proposed for the specified problems as shown in fig.3.

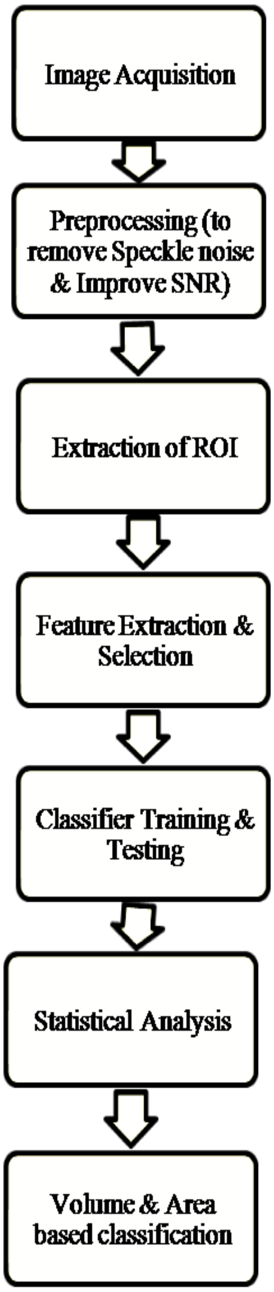

Fig-3: Process Flowchart.

There are many modalities by which images of fundus images could be acquired. One such modality is the Optical Coherence Tomography (OCT). Sample images (Normal and Abnormal) are shown in fig. 4.

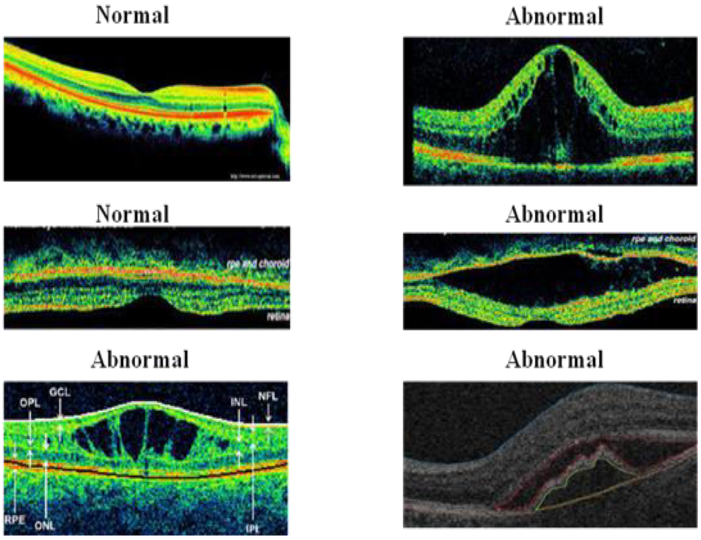

Fig-4: Normal and Abnormal Images of OCT [13][21][31].

The images acquired using this modality of imaging are more prone to speckle noises as ultra sound is used as a source to obtain the image. Speckles are not only noise generating in nature but also information carrying in various high scattering biological tissues. Irrespective of the relation with the surface texture, the dark and bright spots in the images vary even for a small movement in the surface. Mutually coherent reflected waves interfere with each other thereby generating speckles. Sources of speckles include, multiple backscattering of the beam within the tissue volume, and random delays of the forward propogating and returning bean caused by multiple forward scattering. The above mentioned sources generate constructive and destructive interferences which inturn lead to formation of the speckles. But these speckle noises are independent of depth. It could be understood that statistical properties of speckles are dominated by the effects of multiple backscatter rather than by the phase abberations incurred during propogation through the overlying tissues. As the speckles contain information as well as noises, care must be taken not to lose the signal informations while reducing the speckle noises. Literatures suggest the usage of median filtering, homomorphic wiener filtering, multiresolution wavelet analysis and adaptive smoothing for reduction of the speckle noises. These techniques could be evaluated in the proposed system. The denoised image can then be subjected to feature extraction techniques, wherein numerous features shall be extracted and optimization needs to be performed in terms of performance and time of computation. Based on the selected features, classification could be performed. Literature supports the use of SVM Classifiers for these images. In addition to this, several other classifiers like k-NN classifiers, Backpropogation Networks can also be evaluated. Any classifier with better performance and lesser time of computation can be selected for the proposed system. After performing the statistical analysis area and volume of the fluid filled region can be calculated, and the abnormal area can be segmented. The segmented image can also be superimposed with the original image in order to present the details of abnormality in a much understandable and clear manner.

Conclusion

It could be seen that the technique implemented for the removal of speckle noises plays a significant role in overall performance of the various systems discussed. Various methods which evolved to three dimensional analyses from two dimensional analyses were discussed in brief. The user friendliness of the system served an essential parameter during the evaluation. It was seen that every system was designed such that it was confined for a single type of disorders. Upto to our knowledge there are no system that can be utilized for a wide range of fluid related abnormalities. Though preprocessing had a key role in all the systems, the ones using textural features for classification had lesser dependency on preprocessing. A system could be developed such that a broader range of fluid related abnormalities could be identified together. Also automations in the therapeutic suggestions could also be integrated thereby forming an Expert System. Since OCT and B mode Ultrasounds are similar, it could be evaluated if a universal system for the similar modalities could be developed.

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