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Survey on Diabetic Retinopathy Detection through Retinal Images

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ABSTRACT

Diabetic retinopathy is an important disease which needs to be diagnosed in earlier to prevent the harmful heart attacks. This paper outlines a brief survey over different techniques developed to diagnose the DR through retinal images. Briefly the earlier approaches are classified into preprocessing and feature extraction techniques. The main objectives f feature extraction techniques is to normalize the retinal image such that it is suitable for analysis and further the feature extraction techniques aims in the extraction of optimal feature set to make the detection system more effective. The pros and cons of all earlier approaches are also discussed in this paper.

Keywords: Diabetic Retinopathy, Optic Disk, Blood Vessel Segmentation, Exudates, datasets.

I. INTRODUCTION

Automation in medical diagnosis is been in investigation from a long time. Researchers have focused on various aspects of medical data to process, towards automation of medical diagnosis, resulting in faster, economical and accurate diagnosis. The primal objective of such system is to overcome the dependency of sample analysis for the captured medical data and process in a supervised manner to extract and detect the effects observed in a given sample. Towards automation, various medical samples, such as MRI, mammogram, x-rays, ECG, EEG etc. are analyzed in online or offline mode. Towards developing automation approach for the detection of Diabetic Retinopathy (DR) through retinal image analysis a similar objective of retinal image diagnosis was also developed [1], [2].

In retinal image analysis, retinal blood vessel segmentation and delineation of morphological attributes such as vessel length, vessel width, tortuosity of vessel and/or branching pattern of vessel and the angle details are utilized for the diagnosis of Diabetic Retinopathy. Automatic detection of retinal vasculature can help in the implementation of diagnosing programs for DR, Evaluation of retinopathy of prematurity [3], fovea avascular region detection [4], arteriolar narrowing [5], the relationship between vessel tortuosity and hypertensive retinopathy [6], vessel diameter measurement in relation with diagnosis of hypertension [7], and computer assisted laser surgery. Further the automatic extraction of branch points of vessels and maps of vessels can be used for multimodal or temporal image registration [8], optic disk identification [10] and location of fovea. Finally the retinal vascular structure of every individual is unique; it can be used for biometric identification [11,12].

This paper gives a complete idea about the blood vessel segmentation and all the earlier proposed approaches to achieve. Rest of the paper is organized as follows: section II gives the details of structure of retinal image. Section III gives the details of literature survey. Section IV concludes the paper.

II. LITERATURE SURVEY

Based on the above discussion, the automatic detection of DR involves the extraction of all the fundus image features mentioned above. Hence the literature survey carried out in this paper also follows the same procedure i.e., the approaches focused on the preprocessing are discussed first followed by optic disk segmentation, blood vessel extraction, Exudates detection and finally the classification techniques.

1. Preprocessing

The main objective of preprocessing techniques is to attenuate image variation by normalizing the original retinal image against a reference model or data set for subsequent viewing, processing or analysis.

Because of the acquisition process, very often retinal images are non-uniformly illuminated and exhibit local luminosity and contrast variability. This problem may seriously affect the diagnostic process and its outcome, especially if an automatic computer-based procedure is used to derive diagnostic parameters. A new method is proposed in [14], [15] to normalize luminosity and contrast in retinal images, both intra- and inter-image. The method is based on the estimation of the luminosity and contrast variability in the background part of the image and the subsequent compensation of this variability in the whole image.Due to the complex imaging setup, there is a large luminosity and contrast variability within and across images. Here, [16] use the knowledge of the imaging geometry and proposed an enhancement method for colour retinal images, with a focus on contrast improvement with no introduction of artifacts. The method uses non-uniform sampling to estimate the degradation and derive a correction factor from a single plane. [16]Also proposed a scheme for applying the derived correction factor to enhance all the colour planes of a given image.Furthermore, empirical observations by [17] and [18] identify the green channel of RGB images as containing the maximum contrast. [19] Also note that the green channel appears to provide more information and is less subject to non-uniform illumination. The blue channel contains little useful information for the detection of retinal features.

Histogramequalization redistributes the histogramof each colorchannel in the input image such that the output image contains auniform pixel value distribution. [20] Proposed a method using improved nonlinear hue-saturation-intensity color model (INHSI) to preserve color information of the retinal images. The intensity component is enhanced by Rayleigh transformation in contrast-limited adaptive histogram equalization (Rayleigh CLAHE) [21], [23] algorithm. Redistributing the histogram to match that of a reference image, which does not necessarily contain the lesion, may obscure evidence of the pathology.

Contrast enhancement technique has an important role in the field of retinal image enhancement as it improves the contrast of an image. The contrast is an important factor to differentiate a good quality image from a low quality image.A new retinal image contrast enhancement method for Diabetic Screening System is presented in [22]. The proposed method evaluated by comparing the retinal image quality with different contrast enhancement methods which are applied in numerous papers [24, 25]. The proposed method produces better image quality and also preserves the mean brightness of the input images which is very important for medical image analysis.[19] Proposed a multilevel histogram equalization (MLE) method as a preprocessing step in the detection of drusen. The approach is based on the sequential application of histogram equalization to progressively smaller non-overlapping neighborhoods. The size of the neighborhood is always larger than the target lesion. However, the detection of multiple types of anatomy and pathology with different physical dimensions is also problematic when relying upon a hierarchal neighborhood method.

2. Optic Disk (OD) Segmentation

Segmentation of the optic disk usually refers to the subsequent task of determining the contour of the disk. Localization and segmentation of the optic disk are important tasks in retinal image analysis. The disk centre and contour are often prerequisite landmarks in establishing a frame of reference for identifying Diabetic Retinopathy.Related work regarding the OD detection using fundus images can be broadly categorized into two groups based on: the shape, color, and structure of the OD, and the properties of the retinal vasculature. The automated algorithms belonging to both the categories are discussed as follows.

2.1 Structural Features based OD detection

This category includes the well-known methods that rely on the appearance and size of the OD [26], such as the method in [27] that detects bright regions by mathematical morphology and detects the OD as the largest high contrast average circular-shape area. The method in [28] uses morphology followed by watershed transform for the model-based OD detection. The method in [42] first locates a pixel belonging to the OD region, and then applies boundary segmentation by morphology, edge detection, and circular Hough transforms. Other well-known methods in [29] and [30] use a line operator to capture the circular brightness structure of the OD since the maximum and minimum variation along the linear operator has a specific pattern to locate the OD.

2.2 Retinal Vasculature based OD detection

This category of methods examine the retinal vasculature for locating the OD, since the OD is the point of entrance of the optic nerve and blood vessels which branch out into finer vessels through the retina. The method in [26] applies a search on the branching network patterns formed by the blood vessels to converge to the region where most paths ended, followed by the application of Hough transform on all such regions to finally locate the OD.

Another method in [31] matches directional patterns of the retinal blood vessels to match the direction of OD vicinity. The method in [32] localizes the OD by tracking the blood vessels using Gabor filters to detect the peaks in nodes via phase portrait analysis and locates the OD at the focal point of the vessels using Hough transform. The method in [33] applies watershed transform for detecting the OD location and disc boundary using the information regarding the major vessel arcade. Besides, maximization of vessel pattern-based entropyis used to detect the location of the OD in [34].

2.3 Combined Strategies

Some algorithms, however, have combined the two categories, such as the method in [35] that locates the OD based on the structure of the OD, the convergence of blood vessels at the OD, and the variation in the size of the blood vessels entering the OD. Another method in [36] uses the feature-based k-nearest neighbor classifier for training and extracting the OD. The method in [43] uses an ensemble of pyramidal decomposition, edge detection, entropy-filter-based detection, Hough transform, and feature-vector-based algorithms for detecting the OD. Another method in [37] uses the principal component image plane followed by the removal of vessel regions, image inpainting, stochastic watershed transform, and regional discrimination for the OD boundary detection. Also, the method in [44] applies super-pixel classification to separate pixels of the disc from non-discs using histogram and center surround statistics.

III. RETINAL BLOOD VESSEL EXTRACTION

The segmentation and measurement of the retinal vessels is of primary interest in the diagnosis and treatment of a Diabetic Retinopathy. As previously discussed, the accurate segmentation of the retinal blood vessels is often an essential prerequisite step in the identification of retinal disorders and abnormalities.The vessel cross-sectional intensity profiles approximate a Gaussian shape or a mixture of Gaussians in the case where a central vessel reflex is present. The orientation and grey level of a vessel does not change abruptly; they are locally linear and gradually change in intensity along their lengths. The vessels can be expected to be connected and, in the retina, form a binary treelike structure. However, the shape, size and local grey level of blood vessels can vary hugely and some background features may have similar attributes to vessels. Vessel crossing and branching can further complicate the profile model. As with the processing of most medical images, signal noise, drift in image intensity and lack of image contrast pose significant challenges to the extraction of blood vessels.

In earlier so many approaches are proposed to perform retinal vasculature segmentation based on various aspects like curvature of vessel, morphological operations, matched filtering etc. This section gives a complete knowledge about the earlier proposed retinal vascular segmentation approaches.

3.1 Curvature based methods

In this case, the blood vessel can be modeled as a curve for smoother extraction. Along with this, the abnormalities in the blood vessels can be determined through the tortuosity of the vessels. Tortuosity is an indication of how winding a blood vessel is [45]. If there is more tortuosity in the blood vessel there may be chance of DR. Tortuosity can be happen in small portions of blood vessel or throughout the blood vessel network.

3.1.1. Arc Length over Chord Length Ratio Methods

Methods of this group have simple mathematical expressions. The first methods of this categorywass introduced in [46] and was widely utilized thereafter (e.g.,[47]–[50]). However, it is apparent that the arc over chord length ratio, on its own, is insufficient for determination of vessels with smooth curvature and vessels with variation in curvature direction. For compensation, [51] and [52] proposed modifications on the approach. In [52], vessels are partitioned into segments with the same convexity and a weighted sum of arc over chord length of all segments is proposed as a tortuosity measure.

3.1.2. Methods Based on Curvature

Curvature is a mathematical measure for howinflected a curve is at a certain coordinate. The author of [48] uses curvature to propose two tortuosity measures which are the integral of curvature and the integral of curvature squared. Moreover, the ratio of these integrals over arch or chord length has also been proposed as tortuosity measures in [48]. In [53], the integral of squared curvature derivative is suggested as a measure of tortuosity. These or other curvature-based algorithms have been used in most of the recent works including [54], [55] as well. Curvature based tortuosity measures are more reliable, but they impose a heavy computational burden compared to the methods of the first group.

3.1.3. Methods Based on Angle Variation

These methods compute the direction variations of the vessel to measure tortuosity. In [56], the average of the angles between sample center points that describe the vessel (called local direction variation) was used to measure tortuosity. In [57], the same method is used to measure local angles and the number of times a local angle surpasses 30^0 is considered as tortuosity index.

3.1.4. Methods Based on Other Domain

These methods are in fact a subgroup of the curvature-based methods. The difference is that unlike the first group, they calculate curvature in domains beside the space domain. [58] Used Fourier analysis and [59] used circular Hough transform to calculate curvature. Moreover, in [60],Non-Subsampled Contourlet Transform is used for curvature calculation. The key feature of these methods is evaluation of tortuosity without vessel extraction. However, they suffer from heavy computational burden as well. There have also been some special cases of tortuosity measurement algorithms. For example, [61] used cubic-spline interpolation for measuring tortuosity.

3.2 Morphological based methods

Morphological processing which consist of techniques dealing with digital image processing using mathematical morphology by applying some structure element (SE) to binary images and sometimes to gray-level images.

A novel three-stage blood vessel segmentation algorithm was developed in [62]. The first stage is pre-processing by high-pass filtering then extracting a binary image and another binary image is reconstructed from morphologically enhanced image for the vessel regions. Next the major vessels are extracted which is common regions from these two images. Then the second stage, Gaussian Mixture Model (GMM) classifier is used to classify all pixels in the two binary images which are remained from previous stage.Morphological multi-scale enhancement method is also presented in [64]. For the extraction of the blood vessels in the angiogram; fuzzy filter and watershed transformation are used.In the method [65] an approach is presented which is combined unique vessel centerlines detection with morphological bit plane slicing. The first order derivative of a Gaussian filter is used in four directions to extract the centerlines, and then performing an average derivative and derivative signs with the extracted centerlines. Morphological multidirectional top-hat operation is applied on blood vessels gray-scale image with linear structure element to obtain the orientation map and shape. In [66] fast discrete curvelet transform with multi-structure mathematical morphology is proposed. For detecting the blood vessels edges, multi-structure morphological transformation is applied. Then morphological opening is applied on the result image to remove the false edges. An automated enhancement and segmentation method for blood vessels is presented in [67]. This method decreases the optic disc influence and emphasizes the vessels by applying a morphological multidirectional top-hat transform with rotating structuring elements to the background of the retinal image.

IV. CONCLUSIONS

In this paper, a brief literature survey is carried out over the approaches developed to perform automatic detection of Diabetic Retinopathy. Based on objectives of earlier developed approaches, totally they are classified into four classes. They are preprocessing approaches, optic disk segmentation approaches, Retinal blood vessel extraction techniques and supervised classification techniques. Various approaches proposed by various authors aimed to optimize the accuracy of system by focusing towards these objectives. All the approaches are tested over standard databases as already mentioned in the paper and the performance is evaluated through the performance metrics Accuracy, Sensitivity and Specificity.

V. REFERENCES

[1]. Mr. SangmeshBiradar, Prof. A.S.Jadhav, "A Survey on Blood Vessel Segmentation and Optic Disc Segmentation of Retinal Images", International Journal of Advanced Research in Computer and Communication Engineering Vol. 4, Issue 5, 2015.

[2]. T. Teng, M. Lefley, D. Claremont, "Progress towards automated diabetic ocular screening: a review of image analysis and intelligent systems for diabetic retinopathy", Medical and Biological Engineering and Computing Vol.40, pp.2-13, 2002.

[3]. C. Heneghan, J. Flynn, M. O'Keefe, M. Cahill, "Characterization of changes in blood vessel width and tortuosity in retinopathy of prematurity using image analysis", Medical Image Analysis, Vol.6, pp.407-429, 2002.

[4]. A. Haddouche, M. Adel, M. Rasigni, J. Conrath, S. Bourennane, "Detection of the foveal avascular zone on retinal angiograms using Markov random fields", Digital Signal Processing,Vol.20, pp.149-154, 2010.

[5]. E. Grisan, A. Ruggeri, "A divide et impera strategy for automatic classification of retinal vessels into arteries and veins", Proceedings of the 25th IEEE Annual International Conference in Engineering in Medicine and Biology Society, vol. 891, pp. 890-893, 2003.

[6]. M. Foracchia, "Extraction and quantitative description of vessel features in hypertensive retinopathy fundus images", 2nd International Workshop on Computer Assisted Fundus Image Analysis, 2001.

[7]. J. Lowell, A. Hunter, D. Steel, A. Basu, R. Ryder, R.L. Kennedy, "Measurement of retinal vessel widths from fundus images based on 2-D modeling", IEEE Transactions on Medical Imaging, Vol.23, pp.1196-1204, 2011.

[8]. F. Zana, J.C. Klein, "A multimodal registration algorithm of eye fundus images using vessels detection and Hough transform", IEEE Transactions on Medical Imaging,Vol.18,pp.419-428, 1999.

[9]. K. Fritzsche, A, Can, H. Shen, C. Tsai, J. Turner, H.L. Tanenbuam, C.V. Stewart, B. Roysam, J.S. Suri, S. Laxminarayan, "Automated model based segmentation, tracing and analysis of retinal vasculature from digital fundus images", in: State-of-The-Art Angiography, Applications and Plaque Imaging Using MR, CT Ultrasound and X-rays, Academic Press, pp. 225-298, 2003.

[10]. L. Huiqi, O. Chutatape, "Automated feature extraction in color retinal images by a model based approach, IEEE Transactions on Biomedical Engineering, Vol.51, pp.246-254, 2004.

[11]. C. Marin˜ o, G. Penedo, M. Penas, J. Carreira, F. Gonzalez, "Personal authentication using digital retinal images", Pattern Analysis and Applications, Vol.9, pp.21-33, 2006.

[12]. C. Köse, C. Ikibas, "A personal identification system using retinal vasculature in retinal fundus images", Expert Systems with Applications, Vol.38, pp.13670-13681, 2011.

[13]. B. Cassin, S.A.B. Solomon, Dictionary of Eye Terminology, 2nd ed., Triad Publishing Company, 1990.

[14]. Foracchia M, Grisan E, Ruggeri A,"Luminosity and contrast normalization in retinal images", Med Imaging Anal, Vol.9, pp.179-90, 2005.

[15]. Ehsan S, "Luminosity and contrast normalization in color retinal images based on the standard reference image", Proc. SPEI 9784, Medical Imaging, 2016.

[16]. GopalDutt Joshi, "Colour Retinal Image Enhancement based on Domain Knowledge", Proc. of the IEEE Sixth Indian Conference on Computer Vision, Graphics and Image Processing (ICVGIP 2008),pp. 591-598, 2008, Bhubaneswar, India.

[17]. Shin DS, Javornik NB, Berger JW, "Computer-assisted, interactive fundus image processing for macular drusen quantitation", Ophthalmology, Vol.106, pp.1119-25, 1999.

[18]. Leandro JJG, Soares JVB, Cesar Jr RM, Jelinek HF, "Blood vessels segmentation in non-mydriatic images using wavelets and statistical classifiers, In: XVI Brazilian symposium on computer graphics and image processing, p.262-9, 2003.

[19]. Rapantzikos K, Zervakis M, Balas K, "Detection and segmentation of drusen deposits on human retina: potential in the diagnosis of age-related macular degeneration", Med Imaging Anal,Vol.7, pp.95-108, 2003.

[20]. Thani, "Color retinal image enhancement by Rayleigh contrast-limited adaptive histogram

equalization", 14th International Conference on Control, Automation and Systems (ICCAS), 2014.

[21]. T.Jintasuttisak, S.Intajag, "Color Retinal Image Enhancement by Rayleigh Contrast-Limited Adaptive Histogram Equalization", 14th International Conference on Control, Automation and Systems, Korea, pp. 22-25, 2014.

[22]. N.S.Datta, "A new contrast enhancement method of retinal images in Diabetic Screening System", IEEE 2nd International Conference on Recent Trends in Information Systems (ReTIS), 2015

[23]. Saikat Kumar Shome, "Enhancement of Diabetic Retinopathy Imagery Using Contrast Limited Adaptive Histogram Equalization", International Journal of Computer Science and Information Technologies, Vol.2, pp.2694-2699, 2011.

[24]. J. A Stark, "Adaptive Image Contrast Enhancement Using Generalizations of Histogram Equalization", IEEE Transactions on Image Processing, Vol.9, pp.889-894, 2000.

[25]. Ni M Noor, N Abdul Khalid, Mohd Ali, Alice D Numpang, "Fish Bone Impaction Using Adaptive Histogram Equalization (AHE)", Second International Conference on Computer Research and Development, IEEE Computer Society, 2010.

[26]. F. ter Haar, "Automatic localization of the optic disc in digital colour images of the human retina," M.S. Thesis, Dept. Comput.Sci., Utrecht University, Utrecht, the Netherlands, 2005.

[27]. A. Sopharak, B. Uyyanonvara, S. Barman, and T. H. Williamson, "Automaticdetection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods," Comput. Med. Imag. Graph.,Vol. 32, pp. 720-727, 2008.

[28]. T.Walter, J.-C. Klein, P.Massin, and A. Erginay, "A contribution of image processing to the diagnosis of diabetic retinopathy-detection of exudates in color fundus images of the human retina," IEEE Transactions on Medical.Imaging, Vol. 21, pp.1236-1243, 2002.

[29]. S. Lu and J.-H.Lim, "Automatic optic disc detection from retinal images by a line operator," IEEE Trans. Biomed. Eng., vol. 58, no. 1, pp. 88-94,Jan. 2011.

[30]. S. Lu, "Accurate and efficient optic disc detection and segmentation by a circular transformation," IEEE Trans. Med. Imag., vol. 30, no. 12, pp. 2126-2133, Dec. 2011.

[31]. A. A. Youssif, A. Z. Ghalwash, and A. S. Ghoneim, "Optic disc detection from normalized digital fundus images by means of a vessels' direction matched filter," IEEE Trans. Med. Imag., vol. 27, no. 1, pp. 11-18, Jan. 2008.

[32]. R. Rangayyan, X. Zhu, F. Ayres, and A. Ells, "Detection of the optic nerve head in fundus images of the retina with Gabor filters and Phase Portrait analysis." J. Digital Imag., vol. 23, no. 4, pp. 438-453, 2010.

[33]. D. Welfer, J. Scharcanski, C. M. Kitamura, M. M. Dal Pizzol, L. W. B. Ludwig, and D. R. Marinho, "Segmentation of the optic disk in color eye fundus images using an adaptive morphological approach," Comput. Biol.Med., vol. 40, no. 2, pp. 124-137, Feb. 2010.

[34]. A. M. Mendonca, A. Sousa, L. Mendonca, and A. Campilho, "Automatic localization of the optic disc by combining vascular and intensity information," Comput. Med. Imag. Graph., Official J. Comput. Med. Imag. Soc., vol. 37, nos. 5/6, pp. 409-417, Sep. 2013.

[35]. M. Goldbaum, S. Moezzi, A. Taylor, S. Chatterjee, J. Boyd, E. Hunter, and R. Jain, "Automated diagnosis and image understanding with object extraction, object classification, and inferencing in retinal images," in Proc. Int. Conf. Image Process., Sep 1996, vol. 3, pp. 695-698.

[36]. M. Niemeijer, M. D. Abrmoff, and B. van Ginneken, "Fast detection of the optic disc and fovea in color fundus photographs," Med. Image Anal., vol. 13, no. 6, pp. 859-870, 2009.

[37]. S. Morales, V. Naranjo, J. Angulo, and M. Alcaniz, "Automatic detection of optic disc based on PCA and mathematical morphology," IEEE Trans. Med. Imag., vol. 32, no. 4, pp. 786-796, Apr. 2013.

[38]. A. Giachetti, L. Ballerini, E. Trucco, and P. Wilson, "The use of radial symmetry to localize retinal landmarks",Comput.Med.Imag. Graph Vol.37, No.56, pp. 369-376, 2013.

[39]. A. Giachetti, L. Ballerini, and E. Trucco, "Accurate and reliable segmentation of the optic disc in digital fundus images," J. Med. Imag., vol.1, no.2, pp. 024001-1-024001-11, 2014.

[40]. D. Zhang andY. Zhao, "Novel accurate and fast optic disc detection in retinal images with vessel distribution and directional characteristics," IEEE J. Biomed. Health Informat., 2014.

[41]. D. Marin, M. E. Gegundez-Arias, A. Suero, and J. M. Bravo, "Obtaining optic disc center and pixel region by automatic thresholding methods on morphologically processed fundus images," Comput. Methods Prog.Biomed., vol. 118, no. 2, pp. 173-185, 2015.

[42]. A. Aquino, M. Gegundez-Arias, and D. Marin, "Detecting the optic disc boundary in digital fundus images using morphological, edge detection, and feature extraction techniques," IEEE Trans. Med. Imag., vol. 29, no. 11, pp. 1860-1869, Nov. 2010.

[43]. R. J. Qureshi, L. Kovacs, B. Harangi, B. Nagy, T. Peto, and A. Hajdu, "Combining algorithms for automatic detection of optic disc and macula in fundus images," Comput. Vis. Image Understanding, vol.116, no.1, pp.138-145, 2012.

[44]. J. Cheng, J. Liu, Y. Xu, F. Yin, D.Wong, N.-M.Tan, D. Tao, C.-Y. Cheng, T. Aung, and T. Y. Wong, "Super pixel classification based optic disc and optic cup segmentation for glaucoma screening," IEEE Trans.Med. Imag., vol. 32, no. 6, pp. 1019-1032, Jun. 2013.

[45]. E. Trucco,H.Azegrouz, and B. Dhillon, "Modeling the tortuosity of retinal vessels: Does caliber play a role?" IEEE Trans. Biomed. Eng., vol. 57, no. 9, pp. 2239-2247, Sep. 2010.

[46]. W. Lotmar, A. Freiburghaus, and D. Bracher, "Measurement of vessel tortuosity on fundus photographs," Albrecht von GraefesArchivF¨urKlinische und ExperimentelleOphthalmologie, vol. 211, no. 1, pp. 49-57, 1979.

[47]. C. Heneghan, J. Flynn, M. OKeefe, and M. Cahill, "Characterization of changes in blood vessel width and tortuosity in retinopathy of prematurity using image analysis," Med. Image Anal., vol. 6, no. 4, pp. 407-429, 2002.

[48]. W. E. Hart, M. Goldbaum, B. Cˆot´e, P. Kube, and M. R. Nelson, "Measurement and classification of retinal vascular tortuosity," Int. J. Med.Informatics, vol. 53, no. 2, pp. 239-252, 1999.

[49]. M. Perez, A. Highes, A. Stanton, S. Thorn, N. Chapman, A. Bharath, and K. Parker, "Retinal vascular tree morphology: A semi-automatic quantification," IEEE Trans. Biomed. Eng., vol. 49, no. 8, pp. 912-917, Aug. 2002.

[50]. P. Benitez-Aguirre,M. E.Craig,M.B. Sasongko, A. J. Jenkins, T.Y.Wong, J. J. Wang, N. Cheung, and K. C. Donaghue, "Retinal vascular geometry predicts incident retinopathy in young people with type 1 diabetes a prospective cohort study from adolescence," Diabetes Care, vol. 34, no. 7, pp. 1622-1627, 2011.

[51]. E. Bullitt, G. Gerig, S. Pizer, W. Lin, and S. Aylward, "Measuring tortuosity of the intracerebral vasculature from MRA images," IEEE Trans. Med. Imag., vol. 22, no. 9, pp. 1163-1171, Sep. 2003.

[52]. E. Grisan, M. Foracchia, and A. Ruggeri, "A novel method for the automatic grading of retinal vessel tortuosity," IEEE Trans. Med. Imag., vol. 27, no. 3, pp. 310-319, Mar. 2008.

[53]. M. Patasius, V. Marozas, A. Lukosevicius, and D. Jegelevicius, "Evaluation of tortuosity of eye blood vessels using the integral of square of derivative of curvature," in Proc. EMBEC, 2005, vol. 5, pp. 20-25.

[54]. R. Crosby-Nwaobi, L. Z. Heng, and S. Sivaprasad, "Retinal vascular calibre, geometry and progression of diabetic retinopathy in type 2 diabetes mellitus," Ophthalmologica, vol. 228, no. 2, pp. 84-92, 2012.

[55]. M. B. Sasongko, T. Y. Wong, T. T. Nguyen, R. Kawasaki, A. J. Jenkins, J. Shaw, C. Robinson, and J. J. Wang, "Serum apolipoproteins are associated with systemic and retinal microvascular function in people with diabetes," Diabetes, vol. 61, no. 7, pp. 1785-1792, 2012.

[56]. K. Chandrinos, M. Pilu, R. Fisher, and P. Trahanias, "Image processing techniques for the quantification of atherosclerotic changes," UK: University of Edinburgh, DAI Res. Paper, 1998.

[57]. K. G. Goh, W. Hsu, M. Li Lee, and H. Wang, "Adris: An automatic diabetic retinal image screening system," Stud. Fuzziness Soft Comput., vol. 60, pp. 181-210, 2001.

[58]. A. Kaupp, H. Toonen, S. Wolf, K. Schulte, R. Effert, D. Meyerebrecht, and M. Reim, "Automatic evaluation of retinal vessel width and tortuosity in digital fluorescein angiograms," Investigative Ophthalmol. Visual Sci., vol. 32, no. 4, pp. 863-863, 1991.

[59]. F. Ghadiri, H. Pourreza, T. Banaee, andM. Delgir, "Retinal vessel tortuosity evaluation via circular hough transform," in Proc. 18th Iranian Conf. Biomed. Eng., Dec. 2011, pp. 181-184.

[60]. F. Ghadiri, S. Zabihi, H. Pourreza, and T. Banaee, "A novel method for vessel detection using contourlet transform," in Proc.Nat.Conf.Commun., Feb. 2012, pp. 1-5.

[61]. D. K. Wallace, S. F. Freedman, and Z. Zhao, "Evolution of plus disease in retinopathy of prematurity: Quantification by roptool," Trans. Amer. Ophthalmological Soc., vol. 107, pp. 47-52, 2009.

[62]. S. Roychowdhury, D. D. Koozekanani , Keshab K and Parhi, "Blood Vessel Segmentation of Fundus Images by Major Vessel Extraction and Sub-Image Classification", in Biomedical and Health Informatics, IEEE Journal, pp. 2168-2194, (2014).

[63]. D. Marn, A. Aquino*, M. Emilio Gegndez-Arias and J. Manuel Bravo, "A new supervised method for blood vessel segmentation in retinal images by using gray-level and moment invariants-based features", in Medical Imaging, IEEE Transactions onl,vol.30,no.1, pp. 146-158, (2011).

[64]. K. Sun , Z. Chen , S. Jiang , and Y. Wang, "Morphological multiscale enhancement, fuzzy filter and watershed for vascular tree extraction in angiogram," Journal of medical systems," in Journal of medical systems,vol.35, pp. 811-824, 2011.

[65]. M.S. Miri and A. Mahloojifar, "An approach to localize the retinal blood vessels using bit planes and center- line detection, " in Computer methods and programs in biomedicine,vol.108, pp. 600-616, 2012.

[66]. M.M. Fraz et al., "Retinal image analysis using curvelet transform and multi-structure elements morphology by reconstruction," in Biomedical Engineering, IEEE Transactions on,vol.58, pp. 1183-1192, 2011.

[67]. Y. Hou, "Automatic Segmentation of Retinal Blood Vessels Based on Improved Multiscale Line Detection," in Journal of Computing Science and Engineering, vol.8, pp. 119-128, 2014.