

A REVIEW ON AUTOMATIC DETECTION OF DIABETIC RETINOPATHY USING DIGITAL FUNDUS IMAGES

Dr. A. Sirajudeen

Associate Professor, Department of Electronics and Communication Engineering, Aurora's Scientific Technological and Research Academy, Hyderabad, Telangana

Abstract- Diabetes is a chronic end organ disease that occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. Over time, diabetes affects the circulatory system, including that of the retina. Diabetic retinopathy is a medical condition where the retina is damaged because fluid leaks from blood vessels into the retina. Ophthalmologists recognize diabetic retinopathy based on features, such as blood vessel area, exudes, hemorrhages, microaneurysms and texture. In this paper we review algorithms used for the extraction of these features from digital fundus images. Furthermore, we discuss systems that use these features to classify individual fundus images. The classifications efficiency of different DR systems is discussed. Most of the reported systems are highly optimized with respect to the analyzed fundus images, therefore a generalization of individual results is difficult. However, this review shows that the classification results improved has improved recently, and it is getting closer to the classification capabilities of human ophthalmologists.

Keywords- Diabetic retinopathy, Fundus images, Automated detection, Blood vessel area, Exudes, Hemorrhages, Microaneurysms, Maculopathy.

I. Introduction

The fast progression of diabetes is one of the main challenges of current health care. The number of people afflicted with the disease continues to grow at an alarming rate. The World Health Organization expects the number of people with diabetics to increase from 130 million to 350 million over the next 25 years [34]. The situation is made worse by the fact that only one half of the patients are aware of the disease. And in the medical perspective, diabetes leads to severe late complications. These complications include macro and micro vascular changes which result in heart disease, renal problems and retinopathy. For example, studies in the United States show that diabetes is the fifth-deadliest disease, and still there is no cure. In the United States, the total annual economic cost of diabetes in 2002 was estimated to be \$132 billion, this translates to one out of every 10 health care dollars spent [10].

Diabetic retinopathy (DR) is a common complication of diabetes. Indeed, it is so common that it is the leading cause of blindness in the working population of western countries [25] The rate of diabetes is increasing, not only in developed countries, but in underdeveloped countries as well. Unfortunately, most developing countries lack basic recording of DR cases [22]. It is estimated that 75% of people with diabetic retinopathy live in developing countries [26]. The situation in developing countries is especially bad, because there is inadequate treatment. Regardless of the health care situation in their country of origin, people with diabetes are 25 times more likely to develop blindness when compared with individuals who do not suffer from this disease [33]. DR is a silent disease, because it may only be recognized by the

patient when the changes in the retina have progressed to a level where treatment is complicated and nearly impossible. The prevalence of retinopathy varies with the age of onset of diabetes and the duration of the disease.

So far, the most effective treatment for DR can be administered only in the first stages of the disease. Therefore, early detection through regular screening is of paramount importance. To lower the cost of such screenings, digital image capturing technology must be used, because this technology enables us to employ state-of-the-art image processing techniques which automate the detection of abnormalities in retinal images.

This paper reviews automated detection systems for DR. This review is structured as follows: First we discuss the underlying disease, i.e. diabetes, in terms of its causes and effects on the human body. Following the goals of this paper, we focus on the effects of diabetes on the eye. These effects lead to features, such as blood vessel area, exudes, hemorrhages, microaneurysms and textures [4]. These features are used for the automatic detection of DR. In the automatic detection of DR stages section we reviewed different automated detection systems which have been reported in scientific literature. In the discussion section we discussed the advantages and disadvantages of different methods. The last section of this paper presents conclusions and outlines further work.

II. Diabetes

Diabetes mellitus (DM) is the name of a chronic, systemic, life-threatening disease. It occurs when the pancreas does not secrete enough insulin or the body is

unable to process it properly. This results in an abnormal increase in the glucose level in the blood. Over time this high level of glucose causes damage to blood vessels. This damage affects both eyes and nervous system, as well as heart, kidneys and other organs [6].

In general there are two types of diabetes. Diabetes type 1 results from a failure of the human body to produce insulin. Type 1 diabetes is less common than type 2 diabetes. People with type 1 diabetes take insulin injections.

It is estimated that 90-95% of Americans, who are diagnosed with diabetes, have type 2 diabetes [1]. This form of diabetes usually develops in adults age 40 and older and is most common in the age group over age 55. About 80% of people with type 2 diabetes are overweight. It was reported that type 2 diabetes is often part of a metabolic syndrome that includes obesity, elevated blood pressure, and high levels of blood lipids [27].

III. Causes

The recent increase in diabetes can be attributed to an aging population and increasing prevalence of obesity as well as sedentary life habits. Genetic inheritance plays a role in both, type 1 and type 2 diabetes. But it appears that type 1 diabetes is also triggered by some (mainly viral) infections. There is also a genetic element in individual susceptibility to some of these triggers which has been traced to particular human leukocyte antigen genotypes. However, even in those who have inherited the susceptibility, type 1 DM seems to require an environmental trigger. Some evidence indicates that the B4 virus might be such a trigger.

A. Effects

Diabetes affects the kidney, eyes, nerves and heart. In the following sections, we have discussed these affects briefly.

a)Diabetic Nephropathy

Diabetic nephropathy is the main cause of end-stage renal diseases. When the body digests protein it contaminates the blood with waste products. The kidneys filter out these waste products. A large number of small blood vessels (capillaries) are an essential component of this filter. After 20-30 years, they start to leak and useful protein is lost in the urine [8].

It was stated that interruption of the renin-angiotensin system slows the progression of renal diseases in patients with type 1 diabetes, but similar data are not available for patients with type 2 [35].

b)Diabetic Cardiomyopathy

Patients with both diabetes and ischemic heart disease seem to have an enhanced myocardial dysfunction

leading to accelerated heart failure (diabetic cardiomyopathy). Thus, patients with diabetes are prone to congestive heart failure [28].

c)Diabetic Neuropathy

Diabetic neuropathy results in a gradual loss of nerve function which limits the amount of sensation on the plantar aspects of the feet [36]. This diminished sensation disables individuals from being able to feel the onset or occurrence of a foot injury. As a result, patients with this disease are more inclined to experience plantar ulceration [36]. People with DM can develop nerve problems at any time, but the longer a person has diabetes, the greater the risk. Acharya et al. state that abnormal plantar pressures play a major role in the pathologies of neuropathic ulcers in the diabetic foot [5].

d)Diabetic Retinopathy

Diabetes mellitus often results in diabetic retinopathy which is caused by pathological changes of the blood vessels which nourish the retina. DR is the main cause of new cases of blindness among adults aged 20–74 years. During the first 20 years of the disease, nearly all patients with type 1 diabetes and >60% of patients with type 2 diabetes have retinopathy. In the Wisconsin Epidemiologic Study of DR, 3.6% of younger-onset patients (type 1 diabetes) and 1.6% of older-onset patients (type 2 diabetes) were legally blind [38]. In the younger-onset group, 86% of blindness was attributable to DR. In the older-onset group, in which other eye diseases were common, one-third of the cases of legal blindness were due to DR. Figure 1 shows the different features of the typical DR image.

DR occurs when the increased glucose level in the blood damages the capillaries, which nourish the retina. As a result of this damage, the capillaries leak blood and fluid on the retina [24]. The visual effects of this leakage are features, such as microaneurysms, hemor-rhages, hard exudates, cotton wool spots or venous loops, of DR [6, 84].

Types of diabetic retinopathy DR can be broadly classified as nonproliferative DR (NPDR) and proliferative DR (PDR). Depending on the presence of specific DR features, the stages can be identified [6, 17]. The following list describes three subclasses of NPDR as well as PDR:

1. Mild NPDR: at least one microaneurysm with or without the presence of retinal haemorrhages, hard exudates, cotton wool spots or venous loops (Fig. 2 (b)).

Approximately 40% of people with diabetes have at least mild signs of diabetic retinopathy [24].

- 2.Moderate NPDR: numerous microaneurysms and retinal haemorrhages are present. A limited amount and cotton

wool spots of venous beading can also be seen (Fig. 2(c)). 16% of the patients with moderate NPDR will develop PDR within 1 year [20].

3. Severe NPDR: is characterized by any one of the following (4-2-1 rule) characteristics: (1) numerous haemorrhages and microaneurysms in 4 quadrants of the retina (2) venous beading in 2 or more quadrants (3) Intraretinal microvascular abnormalities in at least 1 quadrant (Fig. 2(d)). Severe NPDR carries a 50% chance of progression to PDR within 1 year [20].

PDR: is the advanced stage; signals, sent by the retina for nourishment, trigger the growth of new blood vessels. These blood vessels do not cause symptoms or vision loss. But, their walls are thin and fragile, this leads to a high risk that they leak blood (Fig. 2(e)). This leaked blood contaminates the vitreous gel and this causes severe vision loss and even blindness. About 3% of people, with this condition, may experience severe visual loss [12].

IV. Detection Methods

Early detection of DR is important, because treatment methods can slow down the progression of the disease. Most treatment methods are based on laser technology.

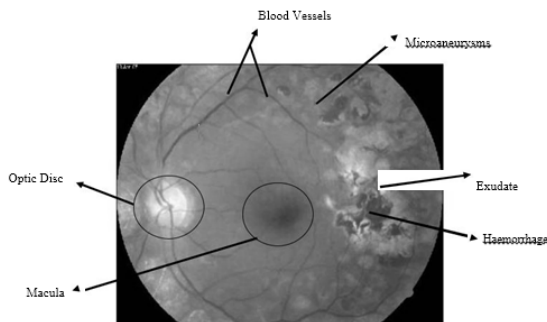


Fig. 1 Different features in a DR image

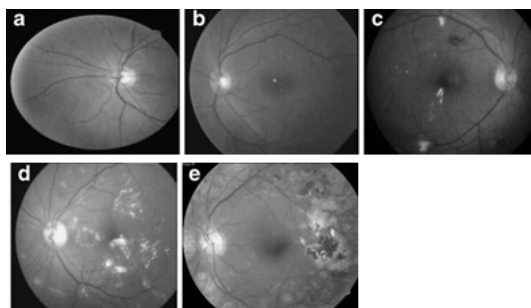


Fig. 2 Typical fundus images: (a) normal (b) mild DR (c) moderate DR (d) severe DR (e) proliferative DR

Laser photocoagulation cauterizes ocular blood vessels, which effectively stops their leakage. The focal laser treatment method reduces retinal thickening. This may prevent worsening of retinal swelling. To be specific, this

treatment reduces the risk of vision loss by 50%. For a small number of cases, with total vision loss, improvement is possible [30].

A. Fundus Images

Medical image analysis is a research area that currently attracts lots of interest from both scientists and physicians. The objective of this field is to develop computational tools which will assist quantification and visualization of interesting pathology and anatomical structures. These tools work with digital fundus images of the eye. The procedure of taking fundus images starts by dilating the pupil with pharmaceutical eye drops. After that the patient is asked to stare at a fixation device in order to steady the eyes. While taking the pictures, the patient will see a series of bright flashes. The entire process takes about five to ten minutes. To ensure that DR treatment is received on time, the eye fundus images of diabetic patients must be examined at least once a year [14].

Image processing can do both reduce the workload of screeners and play a central role in quality assurance tasks. Therefore, there has been an increase in the application of digital image processing techniques for automatic detection of DR [29]. For example, color features on Bayesian statistical classifier were used to classify each pixel into lesion or non-lesion classes [32].

The following sections describe blood vessels, exudes, hemorrhages, microaneurysms and maculopathy detection techniques. These detection techniques yield most of the features which are used in automated DR detection systems.

B. Blood Vessels

Digital fundus photography from the human eye gives clear images of the blood vessels in the retina. This method provides an excellent window to the health of a patient affected by DR. Figure 3 shows an example of blood vessel detection from different types of DR [3]. The blood vessel structure was obtained by subjecting the green component of the RGB fundus image to a number of image processing algorithms [3].

Blood vessels were detected using two-dimensional matched filters [9]. Gray-level profile of cross section of blood vessel approximated by Gaussian shaped curve. The concept of matched filter detection of signals was used to detect piecewise linear segments of blood vessels after the vessel approximation.

Vessel points in a cross section are found with a fuzzy C-means classifier [18]. They have located and outlined blood vessels in images by the use of a novel method to segment blood vessels that compliments local vessel attributes with region-based attributes of the network structure.

Hayashi et al. have developed a computer aided diagnosis system to assist physicians in detecting abnormalities associated with fundus images of the retina [17]. Their proposed system can detect blood vessel intersections and it can identify abnormal widths in blood vessels.

Computerized system for both extraction and quantitative description of the main vascular diagnostic signs from Normal Proliferative

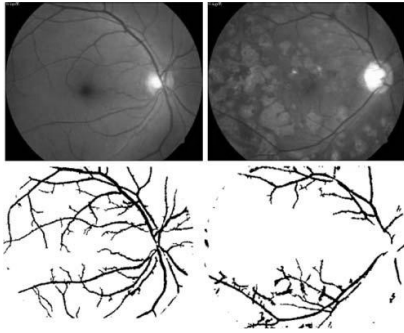


Fig. 3 Results of blood vessel detection for normal and PDR [4]

images in hypertensive retinopathy was presented [23]. The features they have taken into account are vessel tortuosity, generalized and focal vessel narrowing, presence of Gunn or Salus signs.

A new system is proposed for the automatic extraction of the vascular structure in retinal images, based on a sparse tracking technique was proposed [16]. Blood vessel points in a cross section are found by means of a fuzzy c-means classifier. After tracking the vessels, identified segments were connected using greedy connection algorithm. Finally bifurcations and crossings were identified analyzing vessel end points with respect to the vessel structure.

Blood vessel tracker algorithm was developed to determine the retinal vascular network captured using a digital camera [13]. The tracker algorithm detects optic disk, bright lesions such as cotton wool spots, and dark lesions such as haemorrhages. This algorithm identifies arteries and veins with an accuracy of 78.4% and 66.5% respectively.

Vallabha et al. have proposed a method for automated detection and classification of vascular abnormalities in diabetic retinopathy [31]. They detected vascular abnormalities using scale and orientation selective Gabor filter banks. The proposed method classifies retinal images as either mild or severe cases based on the Gabor filter outputs.

The microaneurysms in retinal fluorescein angiograms was identified by first locating the fovea by sub-sampling image by factor of four in each dimension

[11]. Subsequently, the image was subjected to median filtering with a 5 by 5 mask to reduce high-frequency components. Then the image was correlated with a two-dimensional circularly symmetric triangular function with modelled gross shading of the macula.

Blood-vessel detection algorithm based on the regional recursive hierarchical decomposition using quad-trees and post-filtration of edges to extract blood vessels was studied [21]. This method was able to reduce false dismissals of predominately significant edges and faster in comparison to the existing approach with reduced storage requirements for the edge map.

Li et al. have used the arteriolar-to-venular diameter ratio of retinal blood vessels as an indicator of disease related changes in the retinal blood vessel tree [45]. Their experimental results indicate a 97.1% success rate in the identification of vessel starting points, and a 99.2% success rate in the tracking of retinal vessels.

A new method of texture based vessel segmentation to overcome this problem was proposed [7]. The Fuzzy C-Means (FCM) clustering algorithm was used to classify the feature vectors into vessel or non-vessel based on the texture properties. They compared their method with hand-labeled ground truth segmentation for five images and achieved 84.37% sensitivity and 99.61% specificity.

V. Exudates

Exudates are accumulations of lipid and protein in the retina. Typically they are bright, reflective, white or cream colored lesions seen on the retina. They indicate increased vessel permeability and an associated risk of retinal edema. Although, not sight threatening in themselves, they are a marker of fluid accumulation in the retina. However, if they appear close to the macula center they are considered sight threatening lesions. Most of the time they are seen together with microaneurysms. These microaneurysms indicate themselves increased leakage, therefore the classical lesion is a circular ring of exudates with several microaneurysms at its center. Figure 4 shows an example exudates detection from different types of DR [4]. In the result pictures, black indicates no exudates and white indicates the area where exudates were detected. An important step in the extraction process is removing prominent structures of the retina, such as blood vessel tree and optic disc. After these structures have been removed, the exudates were detected using a sequence of image processing algorithms [4].

A novel approach which combines brightness adjustment procedure with statistical classification method and local-window-based verification strategy was proposed [73]. Their results indicate that they were able to achieve 100% accuracy in terms of identifying all the retinal images with exudates while maintaining a 70%

accuracy in correctly classifying the truly normal retinal images as normal.

Hunter et al. have studied neural network based exudates detection [19]. They introduced a hierarchical feature selection algorithm, based on sensitivity analysis to

Normal Proliferative

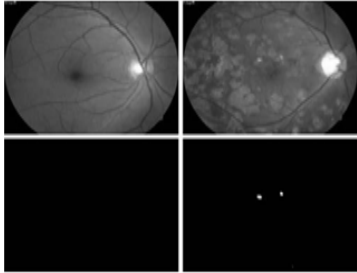


Fig. 4 Results Of Exudates Detection For Normal, PDR

VI. Discussion

The prolonged diabetes leads to the formation of micro-aneurysms and subsequently it leads to exudates as well as haemorrhages. These are the features of DR and they may lead to severe vision loss or even blindness. In order to avoid these complications, it is very important to detect DR early. This can be done by an accurate detection of microaneurysms.

It is very difficult to detect the exudates clearly, because they are tiny spots on the retina. Also, the detection of haemorrhages is very challenging. The texture of haemorrhages and macula is almost the same. So, we need to have robust algorithms which detect these features.

In the previous section we reviewed and compared 15 automated DR detection systems. The results were obtained by optimizing the algorithms for a specific set of fundus images.

In the earlier part of the research, authors have classified into two classes using fundus images based on two or three features. Then subsequently, more features were introduced to improve the classification efficiency. Also, the classification efficiency was improved further by using non-linear methods like higher order spectra [2]. The algorithms involving four features namely, area of blood vessel, exudates, haemorrhages and microaneurysms coupled with support vector machine were used to classify fundus images into five classes (normal, mild DR, moderate DR, severe DR and prolific DR) with an efficiency of 86%, sensitivity and specificity of 82% and 86% respectively [4].

Most of algorithms, discussed in the earlier section, have used only a few features like blood vessels, haemorrhages, exudates and microaneurysms etc. We predict that an algorithm involving all features namely,

blood vessels, exudates, haemorrhages, microaneurysms, distance between exudates and macula, and texture parameters will be more robust. However, for this forecast to hold it is of paramount importance that the individual parameter extraction algorithms are also as robust as possible.

The design of good classifiers will increase the auto-matic detection rate. Huge diverse training data will significantly improve the classification efficiency. Also, fundus images taken under uniform good lighting conditions will improve the detection of DR. Furthermore, different texture parameters along with other DR features can improve the classification efficiency.

The accurate detection of macula, optic disc, microaneurysm and haemorrhages is challenging. But, we feel that, with recent advances in the medical imaging and data mining techniques as well as novel algorithms for the detection of these features, it may be possible.

Also, we feel that, the early detection of the DR (mild DR) by detecting the microaneurysm can save the progression of the disease and hence can save the loss of vision and improve the quality of life.

VII. Conclusion

Prolonged diabetes leads to DR, where the retina is damaged due to fluid leaking from the blood vessels. Usually, the stage of DR is judged based on blood vessels, exudates, hemorrhages, microaneurysms and texture. In this paper, we have discussed different methods for features extraction and automatic DR stage detection. An ophthalmologist uses an ophthalmoscope to visualize the blood vessels and his or her brain to detect the DR stages. Recently digital imaging became available as a tool for DR screening. It provides high quality permanent records of the retinal appearance, which can be used for monitoring of progression or response to treatment, and which can be reviewed by an ophthalmologist, digital images have the potential to be processed by automatic analysis systems. A combination of both accurate and early diagnosis as well as correct application of treatment can prevent blindness caused by DR in more than 50% of all cases. Therefore, regular screenings for DR of patients with diabetes is important. The grading of the resultant fundus images is an important cost factor. Automated DR detection can reduce the grading cost and thereby make the whole screening process less expensive. Some of the algorithms and systems reviewed in this paper are close to achieve DR identification in clinical practice.

References

- [1] Aboderin, I., Kalache, A., Ben-Shlomo, Y., Lynch, J. W., Yajnik, C. S., Kuh, D., and Yach, D., Life course perspective on coronary heart disease: key

- issues and implications for policy and research. World Health Organization, Geneva, 2002.
- [2]. Acharya, U. R., Chua, K. C., Ng, E. Y. K., Wei, W., and Chee, C., Application of higher order spectra for the identification of diabetes retinopathy stages. *J. Med. Syst.*, USA 32(6):431–488, 2008.
- [3]. Acharya, U. R., Lim, C. M., Ng, E. Y. K., Chee, C., and Tamura, T., Computer based detection of diabetes retinopathy stages using digital fundus images. *J. Eng. Med.* 223(H5):545–553, 2009.
- [4]. Acharya, U. R., Lim, C. M., Ng, E. Y. K., Chee, C., and Tamura, T., Computer-based detection of diabetes retinopathy stages using digital fundus images. *Proc Inst Mech Eng H.* 223(5):545–553.
- [5]. Acharya, U. R., Ng, E. Y. K., and Suri, J. S., Image modelling of human eye. Artech House, MA, 2008.
- [6]. Alberti, K. G., and Zimmet, P. Z., Definition, diagnosis and classification of diabetes mellitus and its complications, part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet. Med.* 15(7):539–553, 1998.
- [7]. Bhuiyan, A., Nath, B., Chua, J., and Kotagiri, R., Blood vessel segmentation from color retinal images using unsupervised texture classification. *IEEE Int. Conf. Image Processing, ICIP 5:*521–524, 2007.
- [8]. Brenner, M. B., Cooper, E. M., de Zeeuw, D., Keane, F. W., Mitch, E. W., Parving, H. H., Remuzzi, G., Snapinn, M. S., Zhang, Z., and Shahinfar, S., Effects of Losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *NEJM* 345(12):861–869, 2001.
- [9]. Chaudhuri, S., Chatterjee, S., Katz, N., Nelson, M., and Goldbaum, M., Detection of blood vessels in retinal images using two-dimensional matched filters. *IEEE Trans. Med. Imag.* 8(3):263–269, 1989.
- [10]. Cigna healthcare coverage position- A Report, 2007. Retrieved from: http://www.cigna.com/customer_care/healthcare_professional/coverage_positions/medical/mm_0080_coveragepositioncriteria_ima_ging_systems_optical.pdf. Last accessed on 5th December 2007.
- [11]. Cree, J. M., Leandro, J. J. G., Soares, J. V. B., Cesar, R. M. Jr., Jelinek, H. F., and Cornforth, D., Comparison of various methods to delineate blood vessels in retinal images, Proceedings of the 16th Australian Institute of Physics Congress, Canberra, 2005.
- [12]. Diabetic Retinopathy. Retrieved from: <http://www.hoptechno.com/book45.htm>. Last accessed on 17th January 2009.
- [13]. Englmeier, K. H., Schmid, K., Hildebrand, C., Bichler, S., Porta, M., Maurino, M., and Bek, T., Early detection of diabetes retinopathy by new algorithms for automatic recognition of vascular changes. *Eur. J. Med. Res.* 9(10):473–488, 2004.
- [14]. Fong, D. S., Aiello, L., Gardner, T. W., King, G. L., Blankenship, G., Cavallerano, J. D., Ferris, F. L., and Klein, R., Diabetic retinopathy. *Diabetes Care* 26(1):226–229, 2003.
- [15]. Frank, R. N., Diabetic retinopathy. *Prog. Retin. Eye Res.* 14 (2):361–392, 1995.
- [16]. Grisan, I. E., Pesce, A., Giani, A., Foracchia, M., and Ruggeri, A., A new tracking system for the robust extraction of retinal vessel structure, 26th Annual International Conference of the IEEE EMBS San Francisco, USA, pp. 1620-1623, 2004.
- [17]. Hayashi, J., Kunieda, T., Cole, J., Soga, R., Hatanaka, Y., Lu, M., Hara, T., and Fujita, F., A development of computer-aided diagnosis system using fundus images, Proceeding of the 7th International Conference on Virtual Systems and MultiMedia (VSMM 2001), pp. 429-438, 2001.
- [18]. Hoover, A. D., Kouzanetsova, V., and Goldbaum, M., Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response. *IEEE Trans. Med. Imag.* 19(3):203–210, 2000.
- [19]. Hunter, A., Lowell, J., Owens, J., and Kennedy, L., Quantification of diabetic retinopathy using neural networks and sensitivity analysis, In Proceedings of Artificial Neural Networks in Medicine and Biology, pp. 81-86, 2000.
- [20]. International Council of Ophthalmology. International standards: international clinical diabetic retinopathy disease severity scale, detailed table. Retrieved from: <http://www.icoph.org/standards/pdrdetail.html>. Last accessed on 17th January 2009.
- [21]. Kandiraju, N., Dua, S., and Thompson, H. W., Design and implementation of a unique blood vessel detection algorithm towards early diagnosis of diabetic retinopathy. Proceedings of the International Conference on Information Technology: Cod-ing and Computing (ITCC'05) IEEE Computer Society, pp. 26-31, 2005.
- [22]. Kumar, A., Diabetic blindness in India: the emerging scenario *Indian J. Ophthalmol.* 46(2):65–66, 1998.

- [23]. Li, H., Hsu, W., Lee, M. L., and Wong, T. Y., Automated grading of retinal vessel caliber. *IEEE Trans. Biomed. Eng.* 52:1352–1355, 2005.
- [24]. Nayak, J., Bhat, P. S., Acharya, U. R., Lim, C. M., and Kagathi, M., Automated identification of different stages of diabetic retinopathy using digital fundus images. *J. Med. Syst., USA*, 32 (2):107–115, 2008.
- [25]. Ong, G. L., Ripley, L. G., Newsom, R. S., Cooper, M., and Casswell, A. G., Screening for sight-threatening diabetic retinopathy: comparison of fundus photography with automated color contrast threshold test. *Am. J. Ophthalmol.* 137(3):445–452, 2004.
- [26]. Orbis. Retrieved from: <http://www.orbis.org>. Last accessed December 2009.
- [27]. Reaven, G. M., Role of insulin resistance in human disease. *Diabetes* 37:1595–1607, 1988.
- [28]. Scott, M., Grundy, C., Benjamin, I. J., Burke, G. L., Chait, A., Eckel, R. H., Howard, B. V., Mitch, W., Smith, S. C., and Sowers, J. R., Diabetes and cardiovascular disease. A statement for Healthcare Professionals From the American Heart Association. *Circulation* 100:1134–1146, 1999.
- [29]. Screening for Diabetic Retinopathy in Europe 15 years after the St. Vincent Declaration. The Liverpool Declaration 2005. Retrieved from: <http://reseauophdiat.aphp.fr/Document/Doc/confliverpool.pdf>. Last accessed on 20th December 2007.
- [30]. Shahidi, M., Ogura, Y., Blair, N. P., and Zeimer, R., Retinal thickness change after focal laser treatment of diabetic macular oedema. *Br J Ophthalmol.* 78(11):827–830, 1994.
- [31]. Vallabha, D., Dorairaj, R., Namuduri, K., and Thompson, H., Automated detection and classification of vascular abnormalities in diabetic retinopathy, *Proceedings of 13th IEEE Signals, Systems and Computers* 2:1625-1629, 2004.
- [32]. Wang, H., Hsu, W., Goh, K. G., and Lee, M., An effective approach to detect lesions in colour retinal images, In *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, 181-187, 2000.
- [33]. Watkins, J. P., ABC of diabetes retinopathy. *British Medical Journal* 326:924–926, 2003.
- [34]. World Diabetes, A newsletter from the World Health Organization, 4, 1998.
- [35]. Samuel, C. L., Elisa, T. L., Yiming, W., Ronald, K., Ronald, M. K., and Ann, W., Computer classification of a nonproliferative diabetic retinopathy. *Arch. Ophthalmol.* 123:759–764, 2005.
- [36]. The American Orthopaedic Foot and Ankle Society, 1999 web page: www.aofas.org/ (Last accessed 21.01.2010).