EARLY PREDICTION OF CEREBROVASCULAR DISEASE USING RETINAL FUNDUS IMAGE

[1]S. Sowmiya, [2]Aishwarya. [2]B, Kalpana.T, [2]Pheny Lawrence
[1]Assistant Professor, [2]B.E. Biomedical Engineering students
[1,2]Rajalakshmi Engineering College
sowmiya.bme@gmail.com

Abstract— Hypertension is one of the major risk factor for occurrence of cerebrovascular diseases (CVS). Earlysymptoms for CVS particularly caused by hypertension can be found in the eye blood vessels. Since the retinal vasculature is similar to the vasculature of the organs like brain and kidneys. It offers a unique and easily accessible window to study the health and dysfunctions of the human body, majorly stroke which can be predicted in the early stages using retinal vasculatures. A retinal fundus image is sufficient for predicting early stages of hypertension which in turn one way or the other may lead to stroke. This study is performed over with two categories (hypertensive and stroke) of patients along with the normal human. In each category, 10 patients were considered and evaluated under the ocular fundus imaging for signs of hypertensive retinopathy. This can tell about the high risk of stroke by locating the retinal arteriovenous (AV) crossing and branch retinal vein occlusion, which is a strong indicator for hypertension. Along with AV crossing, parameters like vessel width and angle between the corresponding crossing blood vessels are found which could pay a way for predicting cerebrovascular diseases. In addition, with the help of Colour Doppler imaging, the orbital vasculature and retinal arterial flow velocities very quickly assessed. Therefore, by comparing the width, angle and resistive index values in both normal and hypertensive retinopathy patient’s fundus images, it is evidently seen that, there is a clear prediction for the risk of stroke.

Index Terms: *AV crossing, Cerebrovascular diseases, Hypertensive retinopathy, Retinal Vasculature, Stroke*

.

1. INTRODUCTION

Cerebrovascular disease (CVS) refers to a group of conditions that affect the circulation of blood to the brain, causing limited or no blood flow to last seconds in areas of the brain. CVS usually termed as stroke which a sudden onset of a neurologic shortfall, because of vascular lesion at particular area. There are three types of stroke namely, in Ischemic stroke; the insufficient oxygen supply is persistent for more than 24 hours. Secondly, in Transient Ischemic Attack (TIA), the insufficient blood supply gets resolved less than 24 hours. The last type is subarachnoid hemorrhage; in which the blood vessel ruptures and leaks in cerebrospinal fluid causing an increase in Intracranial Pressure. The main causes for stroke are Atherosclerosis, embolism and aneurysms. In our research, we have considered the Atherosclerosis, the one of the major cause. Atherosclerosis is a condition where the blood vessel thickens and leads to fibrofatty plaque formation. The fundus of the eye is the only region in the human body where the microcirculation can be observed directly using a normal lens or camera. The diameter of the blood vessels around the optic disc is about 150 µm, and an ophthalmoscope allows observation of blood vessels with diameters as small as 10 µm. Fundus imaging is used to visualize the peripheral and central retina, macula and optic disc along with retinal blood vessels. Changes in the retinal microcirculation seen with aging may indicate hypertension, cardiovascular diseases and stroke. Determining the equivalent width of the arterioles and venules near the optic disc is also a widely used technique to identify cardiovascular risks. Arterial hypertension causes changes in the retinal blood vessels that closely mimic those in brain and can be used to predict stroke. Due to atherosclerosis, in the normal arterio-venous crossing (AV crossing), the blood vessels b ecome thickened and narrowed. This results in compression of the vein that lies beneath the thickened artery causing AV nicking, which resembles a hour glass shape as shown in Fig. 1. Generally the prediction of stroke depends on the nontraditional risk factors and markers of subclinical disease and also on the traditional risk factors which includes current smoking, diabetes mellitus, systolic blood pressure, antihypertensive therapy, prior coronary disease, and left ventricular hypertrophy. With these risk factors stroke can be predicted, but the symptoms with these risk factors are seen only at the later stage, which is very difficult for the patient to survive. To overcome this disadvantage, stroke can be easily predicted at an early stage with the help of retinal microvascular abnormalities, because retinal circulation is the window to the brain circulation. Damage to the retinal circulation may reflect impact of both recognized & unrecognized risk factors, and susceptibility and it stands an Indicator of structural vascular damage.

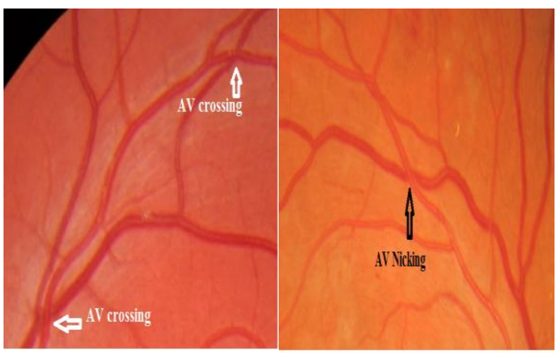

Figure 1: (a) Normal AV Crossing and (b) AV Nicking.

2. METHODOLOGY

The following are the steps performed in this method. Initially the retinal fundus images are obtained using a non-mydriatic fundus camera. These images are pre-processed for extracting the features and the quantification of AV nicking is done by analyzing the parameters such as

- Vessel crossover point detection
- Vessel width measurement
- Angle measurement
- Resistive index

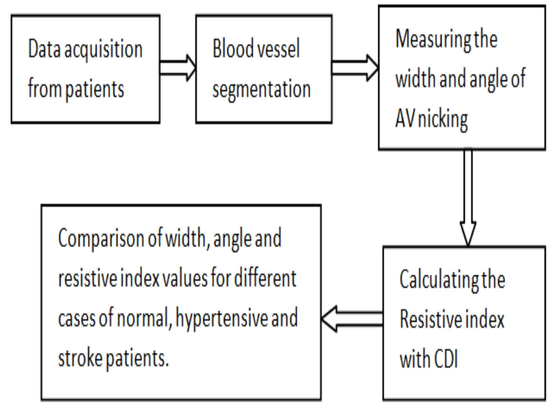

Figure 2: Flow diagram for detection and measurement of width, angle and resistive index

2.1 Vessel Segmentation

For vessel segmentation, we first convert the colour image into a binary image by thresholding. It gives a proper segmentation, enhancement and object detection. From a grayscale image, thresholding can be used to create binary images. The output of the thresholding process is a binary image whose gray level value 0 (black) will indicate a pixel belonging to a print, legend, drawing, or target and a gray level value 1 (white) will indicate the background. The Binarization technique is aimed to be used as a primary phase in various processing and retrieval tasks.

Binarization is often recognized to be one of the most important steps in most high-level image analysis systems, particularly for object recognition. Binarization is a process where each pixel in an image is converted into one bit and you assign the value as '1' or '0' depending upon the mean value of all the pixel. If greater then mean value then its '1' otherwise its '0'. The main advantage of binarization method in blood vessel segmentation is clearly seen and the main and branching blood vessel thickness can be estimated.

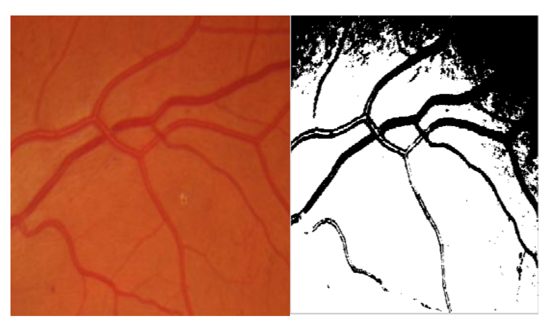

Figure 3: Vessel Binarization

The binarization technique used in retinal blood vessel segmentation as shown in Fig. 3, involves setting of threshold values automatically according to the intensity of the images. Here we have set the two intensity values ranging from 40-100, where if the pixel value is greater than 40, it assigns the value 255, and else the value is 0. A morphological operation is performed “n times” on the binary image until the image doesn’t change. The operation used here is ‘MAJORITY’, in which a pixel value is set to 1, if five or more pixels in its 3-by-3 neighbourhood are 1s; otherwise, it the pixel value is set to 0. As shown in Fig. 4, the skeletonization operation is performed to reduce all objects in an image to lines, without changing the essential structure of the image. For both the operations morphological function is used. Since the skeletons are represented as graph structures, various morphometric parameters such as the branching complexity, the branch length, and the branch diameter are obtained automatically in the blood vessels.

Figure 4: Vessel skeletonization

2.2 Artery-Vein Crossover Point Detection

A crossover point is the place where two vessels (usually a vein and an artery) cross each other while a branching or a bifurcation point is the place where one vessel splits into two vessels. This step aims at identifying the locations of artery-vein crossing (or crossover points) in a retinal image so that their AV nicking severity level can be assessed. This task is achieved by performing an extensive analysis on the vascular skeleton and vascular boundary images which are extracted from the segmented image using morphological operators. From the segmented image, the skeleton image is obtained by a skeletonization process which removes pixels on the boundaries of objects without destroying its connectivity. The vessel boundary image, on the other hand, is achieved by a morphological operator which removes interior pixels and retains only pixels on the vessel boundaries.

2.3 AV Nicking Quantification

Since AV nicking is characterized by the decrease in the venule width at the crossing location, the two vessel segments constituting the vein are extracted and their width measurements are analyzed for AV nicking computation. To achieve this, the segmented image at each crossover point is applied to a sequence of the following steps:

a. Vessel-width measurement
b. Angle of the AV nicking
c. Resistive index measurement

The details of each step are explained in the following section.

a. Vessel Width Measurement

The width of the retinal vessel was determined from digitized fundus photographs by programs based on midpoint detection and boundary tracing. The average vessel width was determined at different distances or eccentricities from the center of the optic disc and using various lengths of vessel segment. In this step, we measure the vessel width along the two segments of the vein, using the vessel skeleton and boundary, extracted in the previous step.

b. Angle of the blood vessel

The angle of the blood vessel is considered as a supporting parameter for detecting the cross-over points in the retinal blood vessels. A crossover point is the place where two vessels (usually a vein and an artery) cross each other. With the help of this, the severity of AV nicking can be assessed easily.

The following values are obtained using the Hough lines:

- The intersecting angles formed by the two vessels at the crossing ($\alpha1$ and $\alpha2$)
- The two angles representing the curvature of each vessel at the crossing ($\beta1$ and $\beta2$).

A crossover point is valid if it satisfies:

$$(\max(\alpha 1, \alpha 2) < \alpha_{max}) \text{ and } (\min(\beta 1, \beta 2) > \beta_{min})$$

c. Resistive index

Resistive index (RI) is an indirect measurement of blood flow resistance that can be used to evaluate vascular damage in ophthalmologic disease. Here we evaluate the RI values of orbital arteries using the color Doppler imaging (CDI) in hypertensive patients with retinopathy leading to cerebrovascular events. CDI is a noninvasive, safe, and useful method, which provides morphologic and vascular information in various diseases. Circulatory parameters in the retro bulbar blood vessels are one of them. Hypertension alters vascular resistance in eyes, and is a major risk factor for arteriosclerosis, and advanced arteriosclerosis occurs with increasing age which indicates long duration of hypertension. The CDI examinations were performed using a Siemens Antares VFX13-5 transducer color Doppler Ultrasound device. The gain was adjusted to avoid art factual color noise, thus allowing detection of low velocities, and the room temperature was brought to optimal level. Scans of the eye were performed in the supine position with head tilted at an angle about 30o, with eyes closed. The transducer was applied to the closed upper eyelid using an ophthalmic sterile gel, with the examiner's hand resting on the orbital margin to minimize the applied pressure to the eye globe and the orbit. Angle of the transducer was taken 30-60 degrees during the examination. After the exclusion of orbital pathologies by B-mod, CDI was performed. The patients were asked to be at the same position for assessing the RI of CRA and PCA and were asked to look the other side during evaluating right or left eye for assessing the RI of OA. Optic nerve was taken as reference for all of the measurements.

Flow through a blood vessel is determined entirely by two factors: the pressure difference between the two ends of the vessel (ΔP) and vascular resistance (R). Resistance refers to the impedance or opposition to blood flow created by the amount of friction the blood encounters as it passes through the vessels and is related to blood viscosity (η), the length of blood vessels (l), and vessel radius (r) (for laminar, no pulsatile fluid flow).

The mathematical formula to determine blood flow (Q) through a vessel can be expressed by modifying Poiseuille's law. The equation is shown as follows.

$$Q=\Delta PR \quad \text{and} \quad R=8\eta l\pi r4 \qquad (1)$$

Peak systolic velocity (PSV; the highest velocity achieved during a systole), end diastolic velocity (EDV; the lowest velocity achieved during a diastole), and resistive index (RI) of assessed vessels were measured for every patient.

The resistive index (RI) is considered to reflect vascular resistance peripheral to the measuring location. RI is derived from the characteristics of the spectral wave form as described by Pourcelot.

The formula for calculating RI is given as,

$$RI= (PSV-EDV)/PSV \qquad (2)$$

Where PSV is peak systolic flow velocity and EDV is end-diastolic flow velocity. The values of RI can vary from 0 to 1, with higher number of greater vascular resistance. The RI values of ophthalmic artery (OA), central retinal artery (CRA), and posterior cilliary artery (PCA) were measured using CDI.

Hence RI might be a useful marker for the ocular hemodynamic of retinal vessels, providing morphologic and vascular information in hypertensive retinopathy.

3. RESULTS AND DISCUSSIONS

A comparative study has been performed in a hospital with three main categories of patients including normal, hypertensive and stroke, along with the vessel width, crossover points, angle and resistive index of the AV crossing present in those blood vessels. We collected 10 patient’s images in each category except stroke patients. Only 6 patients were been able to analyze in stroke category.

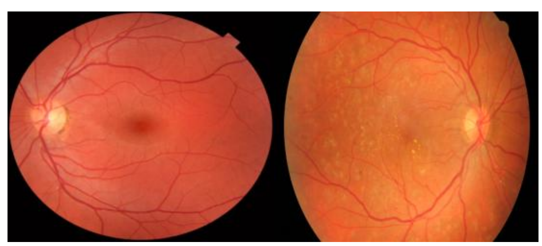

Figure 5: (a) Fundus Image of Normal eye. (b) Fundus image of hypertensive patien

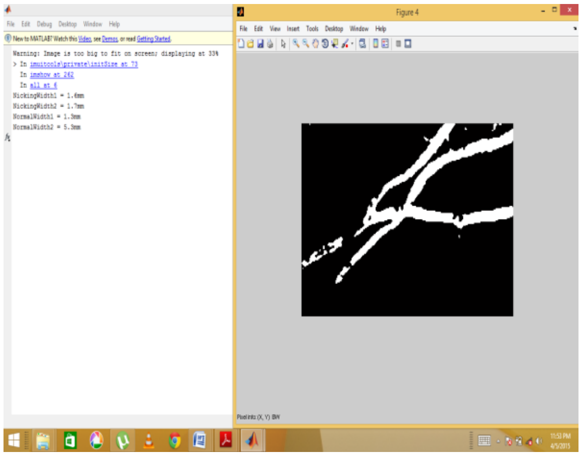

Figure 6: Calculating vessel width of normal eye.

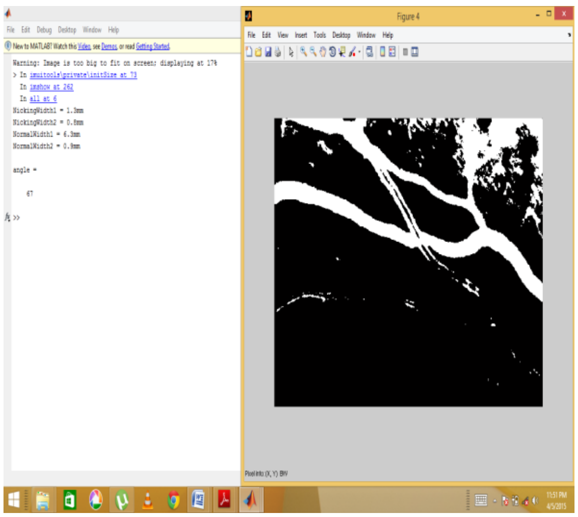

Figure 7: Calculating vessel width of hypertensive patient's eye.

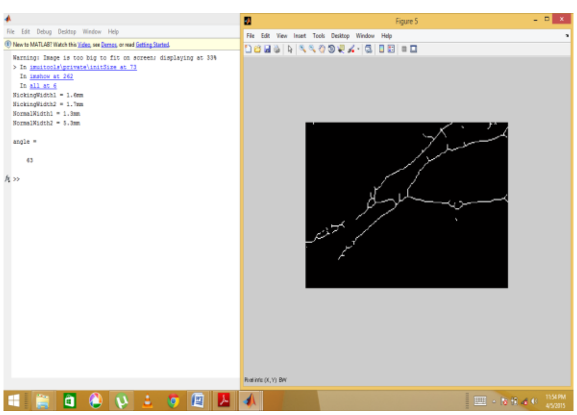

Figure 8: Measuring angles of normal eye.

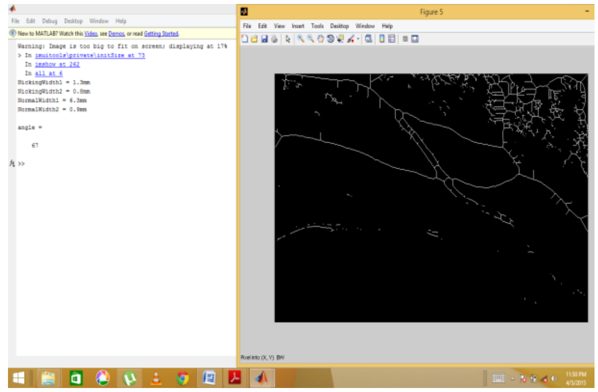

Figure 9: Measuring angles of hypertensive patient's eye.

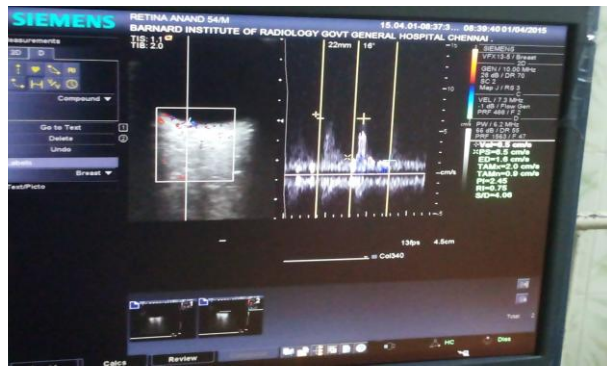

Figure 10: Colour Doppler imaging for Resistive Index. Image courtesy: Rajiv Gandhi General Hospital, Chennai.

Table 1: Comparetive study of parameters with normal, hypertensive and stroke patients.

S. NO	Type of the patient	No of patients	Crossover point number	Width in mm	Angle in θ	Resistive index
1	NORMAL	1	4	2.5	50	0.095
2		2	4	3.7	63	0.072
3		3	3	5.5	69	0.065
4		4	2	4.2	68	0.10
5		5	3	3.5	70	0.092
6		6	2	3.7	63	0.089
7		7	3	4.5	68	0.15
8		8	3	3.5	55	0.12
9		9	4	3.7	74	0.096
10		10	3	4.1	59	0.083
11	HYPERTENSION	1	3	0.6	75	0.66
12		2	3	1.8	76	0.69
13		3	3	1.9	70	0.72
14		4	2	1.8	62	0.70
15		5	3	1.2	84	0.65
16		6	3	1.2	84	0.59
17		7	3	2	72	0.73
18		8	3	0.6	72	0.75
19		9	3	0.7	69	0.64
20		10	3	0.5	70	0.69
21	STROKE	1	4	0.8	87	0.71
22		2	3	0.6	87	0.70
23		3	2	0.5	81	0.75
24		4	2	1.4	88	0.87
25		5	2	1.4	76	0.88
26		6	2	1.0	87	0.81

In this study from table 1, we found that patients with hypertensive retinopathy were associated with stroke risk, by indicating the presence of the retinal micro vascular changes and by evaluating those changes quantitatively. The values of these parameters for different cases are mentioned here. The comparative study of the vessel width, angle and resistive index between normal, hypertensive and stroke patients gave us the combined data collection.

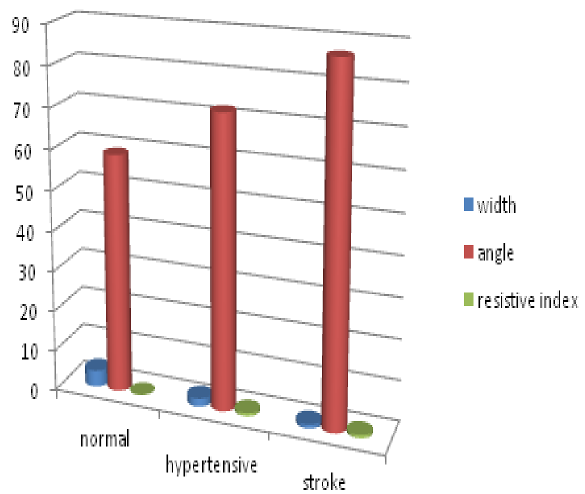

Figure 11: Graph showing the results based on table.

From Table 1 and Fig. 11, The width of the blood vessel for normal patients range from 2-4mm and the angle ranges from 50-70 degree, whereas in case of hypertension and stroke, the width of the blood vessel gets constricted and hence the values range between 0.5-2mm in hypertension and 0.5-1mm in stroke patients. Because of this constriction in width of blood vessel, the angle also changes from acute to obtuse ranging between 60-85 degree in hypertension and 75-90 degree in case of stroke.

Depending upon these three parameters, we can come to the early prediction of stroke. By considering these unique parameters from the retinal blood vessels, it helps the physicians to predict the risk of stroke.

When a clinician pays importance to these three parameters the occurrence of stroke can be predicted at very early stages. Though they are measuring these parameters except angle, but the physicians are not considering it. If they consider these parameters also the early occurrence of stroke can be assessed.

4. CONCLUSION

Due to the constriction of blood vessels, the angle between those vessels also gets wider, which indicate the abnormal change in retinal vasculature. This constriction decreases the vessel width which automatically reduces the blood flow. Because the retinal blood vessels share the same anatomical and physiological characteristics with the cerebral blood vessels, the blood supply to the brain is also affected and this cause blockage in the cerebral blood vessel which leads to stroke.

Therefore, the clinical use of retinal vascular imaging in assessing cerebrovascular risk prediction, will allow the translation of retinal vascular imaging as a tool to improve the diagnosis, prognosis, and management of hypertension in clinical practice.

5. ACKNOWLEDGEMENT

We would like to thank Dr. Sivanyanam, Appaswamy Associates, for his encouragement and support throughout the course of the project and also helping us in data collection through various hospitals. We would like to extend our thanks to Prof. Mrs.Namitha Bhuvaneshwari, Medical director (Regional Institute of Ophthalmology, Government Hospital) and Prof. M.V.S.Prakash for helping us to get patients data. We also like to acknowledge Dr.Mr.Srinivasagalu, Medical director (Rajiv Gandhi government general hospital) for helping us with stroke and hypertensive patients.

REFERENCES

[1] Ali Akal, Turgay Ulas, Tugba Goncu, Ekrem Karakas, Omer Karakas, Fatih Kurnaz, Fatima Nurefsan Boyaci, Omer Faruk Yilmaz, Abdulgafur Bata, and Sema Yildiz 'Evaluation of resistive index using color Doppler imaging of orbital arteries in geriatric patients with hypertension'.

[2] Amanda D. Henderson, M.D., Beau B. Bruce, M.D., M.S., Nancy J. Newman, MD, and Valérie Biousse, MD. 'Hypertension- related eye abnormalities and the risk of stroke' Published in final edited form as Rev Neurol Dis. 2011.

[3] A. Richey Sharrett,Larry D. Hubbard,Lawton S. Cooper, Paul D. Sortie,1 Rosemary J. Brothers, F. Javier Nieto,3 Joan L. Pinsky,1 and Ronald Klein

'Retinal Arteriolar Diameters and Elevated Blood Pressure-The Atherosclerosis Risk In Communities Study'. Received for publication May 12 1998, and accepted for publication December 16, 1998.

[4] Carol Yim-lui Cheung, M. kamran Ikram, Charumathi Sabanayagam, and Tien Yin Wong 'Retinal Microvasculature as a Model to Study the Manifestations of Hypertension' Received June 2, 2012; first decision June 19, 2012; revision accepted August 26, 2012.

[5] Carol Yim-lui Cheung, PhD; Wan Ting Tay, MAppStat; M. Kamran Ikram, MD, PhD; Yi Ting Ong, BSc; Deidre A. De Silva, MRCP; Khuan Yew Chow, MBBCh; Tien Yin Wong, MD, PhD 'Retinal Microvascular Changes and Risk of Stroke-The Singapore Malay Eye Study' Received April 8, 2013; final revision received May 27, 2013; accepted May 29, 2013.

[6] Elz bieta polska, Karl Kircher, Paulina Ehrlich, Pia V.Vecsei, and Leopold Schmetterer 'RI in central retinal artery as assessed but CDI does not correspond to retinal vascular resistance' American Journal of Physiology – Heart and Circulatory Physiology Published 1 April 2001 Vol. 280 no. 4, H1442-H1447 DOI.

[7] F N Doubal, P E Hokke, J M Wardlaw 'Retinal microvascular abnormalities and stroke: a systematic review' Received 8 May 2008, revised 16 September 2008, Accepted 22 September 2008, Published Online First 17 October 2008.

[8] Michelle L. Baker, MD; Peter J. Hand, MD, FRACP; Jie Jin Wang, MMed, PhD; Tien Y. Wong, FRANZCO, PhD 'Retinal Signs and Stroke-Revisiting the Link between the Eye and Brain' Received June 11, 2007; final revision received August 4, 2007; accepted September 13, 2007.

[9] Nidhal, El Abbadi and Enas Al Saadi 'Blood Vessel Diameter Measurement on Retinal Image' Received 2013-08-15; Revised 2013-09-27; Accepted 2014-01-18.

[10] Uyen T. V. Nguyen, Alauddin Bhuiyan, Laurence A. F. Park, Ryo Kawasaki, Tien Y. Wong, Jie J. Wang, Paul Mitchell, Kotagiri Ramamohanarao 'An Automated Method for Retinal Arteriovenous Nicking Quantification from Color Fundus Images'.

[11] Yi-Ting Ong, Tien Y. Wong, Ronald Klein, Barbara E.K. Klein, Paul Mitchell,A. Richey Sharrett, David J. Couper, M. Kamran Ikram 'Hypertensive Retinopathy and Risk of Stroke' Received March 18, 2013; first decision March 30, 2013; revision accepted July 9, 2013.

[12]http://medicaldictionary.thefreedictionary.com/stroke

[13]http://www.nlm.nih.gov/medlineplus/ency/article/000726.htm

[14]http://www.strokecenter.org/patients/aboutstroke/stroke-statistics/