Automated Quantification of Retinal Arteriovenous Nicking from Colour Fundus Images

Uyen T. V. Nguyen, Alauddin Bhuiyan, Laurence A. F. Park, Ryo Kawasaki, Tien Y. Wong, Jie J. Wang, Paul Mitchell, Kotagiri Ramamohanarao

Abstract— Retinal arteriovenous nicking (AV nicking) is the phenomenon where the venule is compressed or decreases in its caliber at both sides of an arteriovenous crossing. Recent research suggests that retinal AVN is associated with hypertension and cardiovascular diseases such as stroke. In this article, we propose a computer method for assessing the severity level of AV nicking of an artery-vein (AV) crossing in color retinal images. The vascular network is first extracted using a method based on multi-scale line detection. A trimming process is then performed to isolate the main vessels from unnecessary structures such as small branches or imaging artefact. Individual segments of each vessel are then identified and the vein is recognized through an artery-vein identification process. A vessel width measurement method is devised to measure the venular caliber along its two segments. The vessel width measurements of each venular segment is then analyzed and assessed separately and the final AVN index of a crossover is computed as the most severity of its two segments. The proposed technique was validated on 69 AV crossover points of varying AV nicking levels extracted from retinal images of the Singapore Malay Eye Study (SiMES). The results show that the computed AVN values are highly correlated with the manual grading with a Spearman correlation coefficient of 0.70. This has demonstrated the accuracy of the proposed method and the feasibility to develop a computer method for automatic AV nicking detection. The quantitative measurements provided by the system may help to establish a more reliable link between AV nicking and known systemic and eye diseases, which deserves further examination and exploration.

I. INTRODUCTION

Arteriovenous nicking (AV nicking or AVN) is one of the most common retinal vascular abnormalities caused by elevated blood pressure (i.e., hypertension) [1]. In response to the increase in blood pressure, the artery becomes stiff, puts pressure on the venule at their common adventitial location (i.e., AV crossing or crossover point) causing nicking at

Uyen T. V. Nguyen is with the Department of Computing and Information Systems, The University of Melbourne, VIC 3010, Australia, e-mail: thivun@student.unimelb.edu.au.

Alauddin Bhuiyan is with the ICT Centre, Commonwealth Scientific and Industrial Research Organization (CSIRO), Australia.

Laurence A. F. Park is with the School of Computing, Engineering and Mathematics, the University of Western Sydney, Australia.

Ryo Kawasaki and Tien Y. Wong are with the Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital, Australia. Tien Y. Wong is also with the Singapore Eye Research Institute, National University of Singapore, Singapore.

Jie J. Wang is with the Centre for Vision Research, Department of Ophthalmology, Westmead Millennium Institute, Australia.

Paul Mitchell is with the Centre for Vision Research, Westmead Millennium Institute, Australia.

Kotagiri Ramamohanarao is with the Department of Computing and Information Systems, the University of Melbourne, Australia.

both sides of the crossing. This phenomenon is called arteriovenous nicking (or *nipping*). In retinal photographs, AV nicking exhibits as the decrease in the venular caliber at both sides of an artery-vein crossing. Figure 1 shows examples of normal and abnormal crossings with the presence of AV nicking. Recent population-based studies [2], [3], [4], [5], [6], [7], [8], [9], [10] have indicated that there is a strong and consistent association between AV nicking and systemic diseases (i.e., stroke and cerebral vascular disorders). In addition, AV nicking was also found strongly associated with retinal vein occlusion, a common sight-threatening ocular disorder [11]. Therefore, the assessment of AV nicking is of clinical importance for the identification of high-risk individuals for early and necessary treatment.

Fig. 1. Examples of artery-vein crossings: (a) a normal AV crossing and (b) an AVN crossing. (Please refer to the colour version of the paper for a clear view of the images.)

Currently, the assessment of AV nicking is done by human (i.e., ophthalmologists or trained graders) on the basis of examples and experience. The degree of narrowing in the venular calibre is used to assess the severity level of AVN, resulting in a 2 (absent or present) or 4 (absent, mild, moderate, or severe) scale grading system. The manual grading, however, is a subjective process as it depends on the graders' expertise and thus, it has many limitations, such as accuracy and reproducibility. The repeatability of AVN assessment in the ARIC study was reported with a fair to moderate agreement (inter and intra-grader kappa value $\kappa = 0.40$ to 0.61 [12] and $\kappa = 0.56$ to 0.57 in a more dedicated study [13]). Hence, an objective grading system with accurate and repeatable measurements is highly desirable. Moreover, manual grading is a tedious and timeconsuming process, which hinders the assessment to be done on large-scale screening for AV nicking detection. Motivated by this, we developed a computer method to quantify the severity of AV nicking, which is to the best of our knowledge, the first system development for AV nicking measurement. The proposed system will help to overcome the limitations of current manual grading process as it provides objective judgment and its measurements are reproducible and repeatable. In addition, the proposed method provides an important basis towards the development of a computer system for automatic AV nicking detection.

II. METHODOLOGY

The proposed system for AV nicking quantification takes as inputs the retinal image and the artery-vein crossing location where the severity level of AVN needs to be assessed and returns a real-number quantifying the AVN severity level of the selected crossover. It consists of 4 main steps: 1) vessel segmentation; 2) artery-vein identification; 3) vessel width measurement; and 4) AV nicking quantification. The following sections describe each step of the system in details.

A. Vessel Segmentation

From the AV crossing location specified by the user, the system first extracts a region of interest (ROI) as a bounding rectangle centered on the target crossover and all subsequent analysis are then performed on the extracted subimage for efficient computation. To extract the blood vessels from the background for further analysis, our previously proposed segmentation technique [14] has been used as it was proven to be effective in dealing with central light reflex problem while providing accurate vessel boundary detection. From the segmented vascular network, a trimming process is performed to isolate the main vessel segments from unnecessary structures such as small branches or noisy artefacts. To achieve this, the system travels from the crossing position through its four connected vessel segments and performs appropriate action when a branching, a crossover, or a bifurcation point is met. A branching point is the place where a vessel branches a small vessel while a bifurcation point is the place where one vessel splits into two vessels. A crossover point is the place where two vessels cross each other. If a crossover or a bifurcation point is met, the system stops its traversal and terminates the vessel along that direction. Otherwise, if a branching point is met, the smaller branch is trimmed off and the system continues its traversal along the main vessel until a bifurcation or a crossover point is encountered. This process helps to retain important vessel structure while removing unnecessary structures to simplify the subsequent analysis. Figure 2 shows the example results obtained through the trimming process on the two crossover points shown in Fig. 1. We can see that this process has effectively removed noisy segments and small branches from the vascular network, retaining only important vessels constituting the crossover. This provides essential results for further analysis for accurate AV nicking assessment.

B. Artery-Vein Identification

The simplified segmentation provides us with a vascular network containing four segments; two associated to the vein and two associated to the artery. Our analysis is performed

Fig. 2. Example results of the vascular network trimming process: (a) initial segmentation; (b) skeleton image (branching point marked with cross signs and bifurcation points marked with circles); (c) segmented image with cut-off at branching and bifurcation points; (d) simplified segmentation.

on the vein, therefore we need to determine which pair is associated to the vein. This is done by an analysis on the vessel skeleton and vessel boundary extracted from the simplified segmentation. The vascular skeleton divides the boundary into 4 sections. For each section, the edge point closest to the crossing position is identified, resulting in 4 edge points: E_1 , E_2 , E_3 , E_4 . Connecting these 4 points in a convex hull order will divide the whole segmentation into 5 parts: the 4 vessel segments and the intersection region. The 4 segments are labeled in a clockwise order from S_1 to S_4 . Then two opposite segments are paired to represent each vessel, i.e., $VSS_1 = (S_1, S_3)$, $VSS_2 = (S_2, S_4)$. Figure 3 depicts this identification process.

Fig. 3. Example showing the individual vessel identification process: (a) the cut-off at the crossover point to separate the vascular network into 4 vessel segments, labelled in a clockwise order (from S_1 to S_4); (b) and (c) two opposite segments are grouped in pair to represent each vessel: $VSS_1 = (S_1, S_3)$, $VSS_2 = (S_2, S_4)$.

The artery-vein (AV) identification process is then performed to distinguish the vein from the artery. For the majority of crossover points, it is observed that the artery appears brighter than its vein counterpart. This is due to the fact that the artery contains oxygenated blood which is pumped from the heart, making it red, while the vein carries de-oxygenated blood back to the heart, which makes it darker. Hence, the color information of the two vessels is computed and the artery is assigned to the vessel with higher intensity value. Different color spaces, RGB and HSV as well as the gray level, were used to identify the most discriminative feature and the green channel has shown to produce highest classification accuracy. Hence, the green channel was used in our system for artery-vein classification. Once the vein is correctly recognized, its two segments are extracted for further analysis.

C. Vessel Width Measurement

In this stage, the system measures the vessel diameters along the two segments of the vein, using the vessel skeleton and boundary, extracted in the previous step. For each skeleton pixel C_i , the two edge points whose connected line is most perpendicular to the vascular skeleton is used to represent the vessel caliber at C_i . The vessel width measurements achieved on two example crossover points (Fig.1) are shown in Fig. 4. We can see that the lines representing the vessel width are perpendicular to the vessel axis while its two edge points are fitted well on the true vessel boundary, which indicates that vessel widths were accurately measured.

Fig. 4. Example results of vessel width measurement produced by the system: imaginary lines connecting two boundary points represent the vessel width at each skeleton pixel.

D. AVN Quantification

As each vein is composed of two segments at two sides of the crossing, the severity of AVN is assessed separately for each segment and the final AVN index of the crossover point is obtained by a combination of these two individual measures. The method for computing the AVN severity level of each venular segment (at one side of the crossing) is as follows. Suppose that the segment is composed of N vessel width measurements: $W = \{w_i | i \in \{1, 2, ..., N\}\}\$ (the vessel widths are indexed and ordered so that w_1 is the width closest to the crossover point, while w_N is the furthest). These measurements are then divided into two sections, $W_C = \{w_i | i \in \{1, 2, \dots, N_C\}\}\)$ consisting of those close to the crossover and $W_F = \{w_i | i \in \{N_C+1, \ldots, N\}\}\$ containing those far from the crossover, where N_C defines the number of measurements in the close section W_C . The AVN severity level of each venular segment is defined as the difference in the vessel width measurements which is far from the crossover and those close to the crossover:

$$
AVN_{V_i} = mean(W_F) - mean(W_C)
$$
 (1)

where *mean* is a function returning the average of the measurements in the specified section, AVN_{V_i} represents the AV nicking severity level computed for the i^{th} venular segment ($i \in \{1, 2\}$). The proposed measure yields high value if there is a decrease in vessel caliber at the crossover (i.e., presence of AV nicking) and low values for normal cases. The final AV nicking level of the crossover point is then computed as the maximum of its two individual measures.

III. EXPERIMENTAL RESULTS

A. Material

The proposed method was evaluated using retinal images obtained from the Singapore Malay Eye Study (SiMES) [15]. These images were captured using the Canon D-60 digital fundus camera with image resolution of 3072×2048 pixels. From this image set, 69 AV crossing points (with varying level of AVN) from 35 retinal images were selected to validate the performance of the proposed method. Each crossing point was manually graded by two experienced graders at the Centre for Eye Research Australia (CERA) (Melbourne, Australia) using 5-scale grading system (from $0 =$ normal to $4 =$ most severe).

B. Results and Discussions

Fig. 5. Performance of the system changes when N_C changes from 5 to 80 pixels. Optimal performance is achieved at $N_C = \{5, 10\}$ with a Spearman coefficient of 0.70.

To assess the performance of the system, the Spearman coefficient was used to measure the correlation between the computed AVN indices and the manual grading. Firstly, to check the dependence of the system performance on the system parameter, N_C , the performance achieved by the system (in terms of Spearman coefficient) when N_C changes from 5 to 80 pixels was examined and plotted in Fig. 5. We can see that the system achieves optimal performance at small values of N_C ($N_C = \{5, 10\}$) and it drops gradually as N_C increases. At the optimal setting, a Spearman coefficient ρ of 0.70 is achieved, which indicates a strong correlation between the computed AVN indices and the manual grading. To visually assess the performance of the system, the AVN indices computed using the proposed measure were plotted against the manual grading and shown in Fig. 6. It is shown that there is a clear linear association between the subjective grading and objective measurements. In addition, it also indicates that the computed values differ from subjective assessment mostly by one grading level, which is reflected by small overlaps in the computed values of two successive grades, while they are well separated for grades of two level apart.

Fig. 6. Box plot showing the linear relationship between the computed AVN index and manual grading.

We note that in the artery-vein identification process, the system can automatically distinguish the vein from the artery with an accuracy of 96.67%. However, since our ultimate goal is to evaluate the accuracy of the AV assessment (the vein must be recognized with an accuracy of 100%), all misclassified points were identified and corrected. This is the only place where the human is needed but this intervention is minimal and indispensable.

IV. CONCLUSIONS

We have proposed and evaluated a new computer system for automated AV nicking quantification. The results show that there is a high correlation between the computed AV nicking values and the manual grading, which has demonstrated the reliability and accuracy of the proposed system for AV nicking assessment. For this study, we assessed the AV nicking level of manually chosen crossover points. In the future, the proposed system will be combined with the crossover point detection system for automatically assessing the AV nicking severity of a whole retinal image. The correlation of the quantified values with known pathologies and diseases is then explored and is the goal of our future research.

ACKNOWLEDGEMENT

The authors wish to thank to Kim Yu Lee and Laurene at the Centre for Eye Research Australia (CERA) (Melbourne, Australia) for having kindly providing us with the arteriovenous nicking grading and clinical advice.

REFERENCES

- [1] T. Y. Wong and P. Mitchell, "Hypertensive retinopathy," *New England Journal of Medicine*, vol. 351, no. 22, pp. 2310–2317, 2004.
- [2] P. Mitchell, J. Wang, T. Wong, W. Smith, R. Klein, and S. Leeder, "Retinal microvascular signs and risk of stroke and stroke mortality," *Neurology*, vol. 65, no. 7, p. 1005, 2005.
- [3] T. Wong, R. Klein, D. Couper, L. Cooper, E. Shahar, L. Hubbard, M. Wofford, and A. Sharrett, "Retinal microvascular abnormalities and incident stroke: the atherosclerosis risk in communities study," *The Lancet*, vol. 358, no. 9288, pp. 1134–1140, 2001.
- [4] T. Wong, R. Klein, B. Klein, J. Tielsch, L. Hubbard, and F. Nieto, "Retinal microvascular abnormalities and their relationship with hypertension, cardiovascular disease, and mortality," *Survey of ophthalmology*, vol. 46, no. 1, pp. 59–80, 2001.
- [5] N. Roper, S. R. Patel, and C. O'Donnell, "Signs of stroke in the retina," *Optometry in Practice*, vol. 13, no. 1, pp. 9–18, 2012.
- [6] T. Wong, R. Klein, A. Sharrett, B. Duncan, D. Couper, B. Klein, L. Hubbard, and F. Nieto, "Retinal arteriolar diameter and risk for hypertension," *Annals of internal medicine*, vol. 140, no. 4, pp. 248– 255, 2004.
- [7] L. S. Cooper, T. Y. Wong, R. Klein, A. R. Sharrett, R. N. Bryan, L. D. Hubbard, D. J. Couper, G. Heiss, and P. D. Sorlie, "Retinal microvascular abnormalities and mri-defined subclinical cerebral infarction the atherosclerosis risk in communities study," *Stroke*, vol. 37, no. 1, pp. 82–86, 2006.
- [8] M. Baker, P. Hand, J. Wang, and T. Wong, "Retinal signs and stroke," *Stroke*, vol. 39, no. 4, pp. 1371–1379, 2008.
- [9] T. Wong and R. McIntosh, "Hypertensive retinopathy signs as risk indicators of cardiovascular morbidity and mortality," *British medical bulletin*, vol. 73, no. 1, pp. 57–70, 2005.
- [10] H. Yatsuya, A. R. Folsom, T. Y. Wong, R. Klein, B. E. K. Klein, and A. R. Sharrett, "Retinal microvascular abnormalities and risk of lacunar stroke atherosclerosis risk in communities study," *Stroke*, vol. 41, no. 7, pp. 1349–1355, 2010.
- [11] R. Klein, B. E. Klein, S. E. Moss, and S. M. Meuer, "The epidemiology of retinal vein occlusion: the beaver dam eye study," *Transactions of the American Ophthalmological Society*, vol. 98, p. 133, 2000.
- [12] L. D. Hubbard, R. J. Brothers, W. N. King, L. X. Clegg, R. Klein, L. S. Cooper, A. R. Sharrett, M. D. Davis, and J. Cai, "Methods for evaluation of retinal microvascular abnormalities associated with hypertension/sclerosis in the atherosclerosis risk in communities study,' *Ophthalmology*, vol. 106, no. 12, pp. 2269–2280, 1999.
- [13] D. J. Couper, R. Klein, L. D. Hubbard, T. Y. Wong, P. D. Sorlie, L. S. Cooper, R. J. Brothers, and F. J. Nieto, "Reliability of retinal photography in the assessment of retinal microvascular characteristics: the atherosclerosis risk in communities study," *American journal of ophthalmology*, vol. 133, no. 1, pp. 78–88, 2002.
- [14] U. T. V. Nguyen, A. Bhuiyan, L. A. F. Park, and K. Ramamohanarao, "An effective retinal blood vessel segmentation method using multi-scale line detection," *Pattern Recognition*, 2012, (DOI: http://dx.doi.org/10.1016/j.patcog.2012.08.009).
- [15] A. W. P. Foong, S. M. Saw, J. L. Loo, S. Shen, S. C. Loon, M. Rosman. T. Aung, D. T. H. Tan, E. S. Tai, and T. Y. Wong, "Rationale and methodology for a population-based study of eye diseases in malay people: The singapore malay eye study (simes)," *Ophthalmic epidemiology*, vol. 14, no. 1, pp. 25–35, 2007.