BIOENGINEERED
2017, VOL. 8, NO. 1, 21–28
http://dx.doi.org/10.1080/21655979.2016.1227144

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

# Optic cup segmentation from fundus images for glaucoma diagnosis

Man Hu[a], Chenghao Zhu[b], Xiaoxing Li[b], and Yongli Xu[b]

[a]National Key Discipline of Pediatrics, Ministry of Education, Department of Ophthalmology, Beijing Children's Hospital, Capital Medical University, Beijing, China; [b]Department of Mathematics, Beijing University of Chemical Technology, Beijing, China

**ABSTRACT**

Glaucoma is a serious disease that can cause complete, permanent blindness, and its early diagnosis is very difficult. In recent years, computer-aided screening and diagnosis of glaucoma has made considerable progress. The optic cup segmentation from fundus images is an extremely important part for the computer-aided screening and diagnosis of glaucoma. This paper presented an automatic optic cup segmentation method that used both color difference information and vessel bends information from fundus images to determine the optic cup boundary. During the implementation of this algorithm, not only were the locations of the 2 types of information points used, but also the confidences of the information points were evaluated. In this way, the information points with higher confidence levels contributed more to the determination of the final cup boundary. The proposed method was evaluated using a public database for fundus images. The experimental results demonstrated that the cup boundaries obtained by the proposed method were more consistent than existing methods with the results obtained by ophthalmologists.

**ARTICLE HISTORY**
Received 11 March 2016
Revised 29 April 2016
Accepted 26 June 2016

**KEYWORDS**
fundus images; glaucoma diagnosis; optic cup segmentation

## Introduction

Glaucoma is a progressive optic neuropathy whose main feature is a structural change in the optic nerve head (ONH), where the optic nerve enters the back of the eyeball. This structural change primarily manifests in the gradual narrowing of the optic disc, indicating the degeneration of optic nerve cells. Since the loss of optic nerve function cannot be restored, early detection and timely treatment of glaucoma are vital to save the patient's vision.[1] The World Health Organization lists glaucoma as the second most common cause of blindness worldwide. According to the glaucoma epidemiologist Quigley, by 2020 the number of glaucoma patients will reach 79.6 million worldwide and 21.8 million in China.[2]

Fundus photography is an important test used in diagnosing glaucoma because it creates an opportunity to assess the retinal ONH structure. In a typical 2-dimensional fundus photograph, the ONH is located within a bright elliptical area. The optic disc is the visible portion of the optic nerve, from which the nerve fibers exit the eye. The central depression of the optic disc is known as the optic cup, and the area around the optic cup is known as the neuroretinal rim. Figure 1 shows the main structures of the ONH.

The cup-to-disc ratio (CDR) and "Inferior, Superior, Nasal, and Temporal" (ISNT) rule are 2 key indicators by which to assess the ONH. The vertical CDR is defined as the ratio of the vertical diameter of the optic cup to the vertical diameter of the optic disc. As glaucoma progresses, optic nerve fibers gradually disappear, thus the optic cup becomes larger with respect to the optic disc, which increases the CDR. In current clinical practice, the CDR is usually obtained via manual measurement by an ophthalmologist. However, depending on the ophthalmologist's experience, the CDR measurement can be affected by subjectivity. Meanwhile, in a normal eye the neuroretinal rim usually follows the ISNT rule: it is thickest at the inferior rim, then the superior rim, then the nasal rim, and it is thinnest at the temporal rim.[3] Because glaucoma causes partial loss of the neuroretinal rim, the rims of glaucoma patients generally do not follow the ISNT rule. Although not all glaucoma patients have the same symptoms, these 2 tests are still very effective in diagnosing glaucoma in a clinic setting.

**CONTACT** Yongli Xu ylxu@mail.buct.edu.cn Wuji Building 216, Beijing University of Chemical Technology, No. 15, Beisanhuandong Road, Chaoyang District, Beijing 100029, China

Color versions of one or more of the figures in this article can be found online at www.tandfonline.com/kbie.

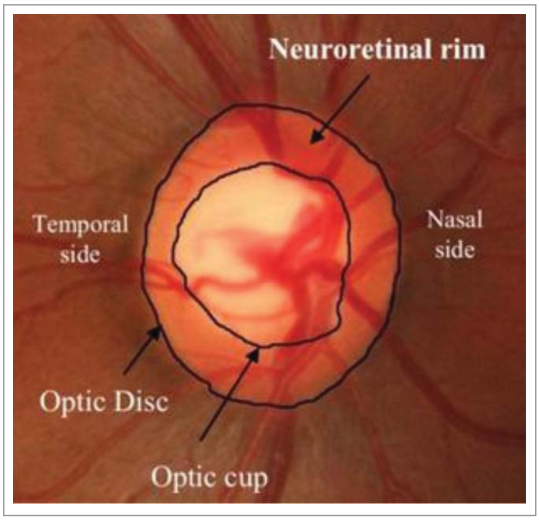


**Figure 1.** Main ONH structures.

Using the CDR and the ISNT rule to perform computer-aided diagnosis of glaucoma has reached a high accuracy rate.[4,5]

However, observing ONH changes manually is a time-consuming process, and its accuracy varies according to the ophthalmologist's experience. Therefore, research is being conducted to determine glaucoma-related structural changes automatically from retinal images. Optic disc and optic cup segmentation are important steps in this process. Optic disc segmentation has achieved highly accurate results that are very close to the results obtained by eye specialists.[6] Relatively, there are few algorithms for optic cup segmentation, and its accuracy is far behind that of optic disc segmentation.

The optic cup has a 3-dimensional structure. Optical coherence tomography (OCT) can be used to reconstruct the optic cup and establish its boundary.[7] In addition, stereoscopic fundus photography can be used to partially reconstruct the 3-dimensional structure of the optic cup and generate the boundary.[8] Nevertheless, fundus photography is more commonly used in eye hospitals and for glaucoma screening. Therefore, it is more practical to reconstruct the optic cup boundary from a fundus image. The algorithms available to draw the optic cup from a fundus image use primarily the following 2 pieces of information: (1) color information in the optic disc, as the optic cup is the gray part of an optic disc; and (2) information about the blood vessel bends in the optic disc. In general, color differs between the inside and outside parts of the optic cup; therefore, points with a high color difference along the optic disc's radial direction can be used as points on the optic cup boundary. Furthermore, blood vessels tend to bend in the vicinity of the optic cup boundary. These vessel bends can also be used to determine the optic cup boundary.

In the early stage, thresholding was used to determine the optic cup boundary, relying on the color intensity difference between the cup and the neuroretinal rim.[9,10] However, this method was valid only in some special cases. Liu et al. proposed a method in which a potential set of pixels belonging to the cup region is first derived based on the reference color obtained from a manually selected point. Next, an ellipse is fitted to this set of pixels to estimate the cup boundary.[11] Joshi et al. used thresholding to determine the set of potential pixels corresponding to the cup boundary and fitted an ellipse based on these pixels.[12] However, the outline obtained via ellipse fitting reflects only coarse cup boundaries. Wong et al. used a level set-based method[13] that relies on the edges between the cup and the neuroretinal rim. Both this method and thresholding-based methods essentially rely on pallor information. However, many fundus images show no obvious pallor or edges within the disc from which to extract the cup boundary. Furthermore, in most fundus images, parts of the optic cup are obviously pallor while other parts are covered with blood vessels and are not obviously pallor. Figure 1 depicts one example of such a disc.

C-means clustering and superpixel classification can also be used for optic cup segmentation. Babu et al. recreated the optic cup through fuzzy C-means clustering on a wavelet-transformed green plane image after the removal of blood vessels.[14] However, the paper did not report the segmentation accuracy of the optic cup. Mittapalli and Kande proposed a clustering-based thresholding algorithm to recreate the optic cup using the spatial distribution of gray levels.[15] Cheng et al. presented a superpixel classification-based method for optic cup segmentation used in glaucoma screening.[16] This method involved computing the center-surround statistics from superpixels and using them with histograms for cup segmentation. Xu et al. extended the superpixel framework by modeling the binary superpixel clustering task as a low-rank representation problem employing the domain prior and the low-rank property of the superpixels.[17] Thorat *et al.* combined clustering and thresholding to segment optic cups.[18] However, the clustering methods and the superpixels methods both fit the optic cup

into an ellipse, ignoring vessel information; therefore, it is easy for them to miss the local features of the optic cup.

Some scholars used small vessel bends or "kinks" in the vicinity of the initially estimated cup boundary to aid cup segmentation.[19] The challenge here was to remove vessel bends in non-boundary areas, especially when the initial estimation was inaccurate. A similar concept has been used to locate relevant vessel bends in the vicinity of a pallor region determined by bright pixels.[20] Hatanaka *et al.* detected two types of vessel bends (visible and invisible bends) and used spline interpolation method to determine the cup boundary.[21] These methods also required pallor information in order to make a good initial estimation of the cup boundary. Moreover, they required at least a few bends in the nasal, inferior, and superior angles of the disc for cup boundary fitting; in practice, these are not necessarily present in many fundus images.

In determining the final optic cup boundary, both of the methods described above focus solely on either color information or blood vessel information, without taking advantage of both sets of information. This paper presents a method for automatic optic cup segmentation that utilizes both color difference and vessel information from fundus images to determine the optic cup boundary. First, this method uses information about the color difference to find an initial cup boundary and give it a local estimate of confidence. Then, based on the initial boundary and the confidence estimate, a vessel bends search area is established, and eventually the related vessel bends are determined. The process of using these 2 sets of information to determine the optic cup boundary not only takes advantage of the position of the points, but also incorporates the confidence of each information point. As a result, this method can effectively integrate 2 types of information and generate optic cup segmentation results that are more consistent than existing methods with results from ophthalmologists' measurements.

## Methods

In practice, an ophthalmologist combines color information and vessel bends to determine the cup boundary. We mimicked this strategy in order to determine the cup boundary, proposing a method to automatically extract the cup boundary by combining the information about color difference and vessel bends. The ophthalmologist relies on the following basic principles: the optic cup boundary is approximately elliptic; the colors inside and outside the optic cup boundary differ noticeably; and blood vessels bend relatively sharply when they pass through the boundary. When conflicts occur between the color difference information and the vessel bends information, the ophthalmologist relies mainly on the more confident information, and considers the other information for support only. For the color difference information, the greater the color difference on the 2 sides of the optic cup boundary, the higher the confidence; in terms of vessel bends, the thicker the bending vessels, the greater the curvature and the higher the confidence. The process by which the ophthalmologist determines the cup boundary involves matching the 2 pieces of information to the model in his or her mind. In imitation of this, the proposed method consists of 3 main processes:

1. Based on the color contrast, the color difference information points and their confidence are determined.
2. Based on the blood vessel information, the vessel bends information points are generated, with confidence provided based on both the vessel diameter and curvature.
3. The above sets of information are integrated to determine the final cup boundary.

Figure 2 shows the proposed method as a flow chart.

During the initial process of determining information points based on color difference, blood vessels might cause interference. This necessitates erasing the blood vessels from the fundus photos. The first step is to extract the vessels from the fundus images. Several methods have been proposed for vessel segmentation in the literature (for a review see ref. 22). This paper followed a morphology-based method[23] to segment the vessels. Then the process of erasing the blood vessels proceeds as follows: for points on the vessels, the color intensities of the given points are replaced by the arithmetic average color intensities of the surrounding non-vascular points, while the color intensities of the non-vascular points remain unchanged. Here, the sounding area of a point is defined as the square with the point as the center and with 19 pixels as the length of each side.

After the removal of the blood vessels, a Chan-Vese active contour model[20] is applied based on the red value of the fundus image in order to determine the

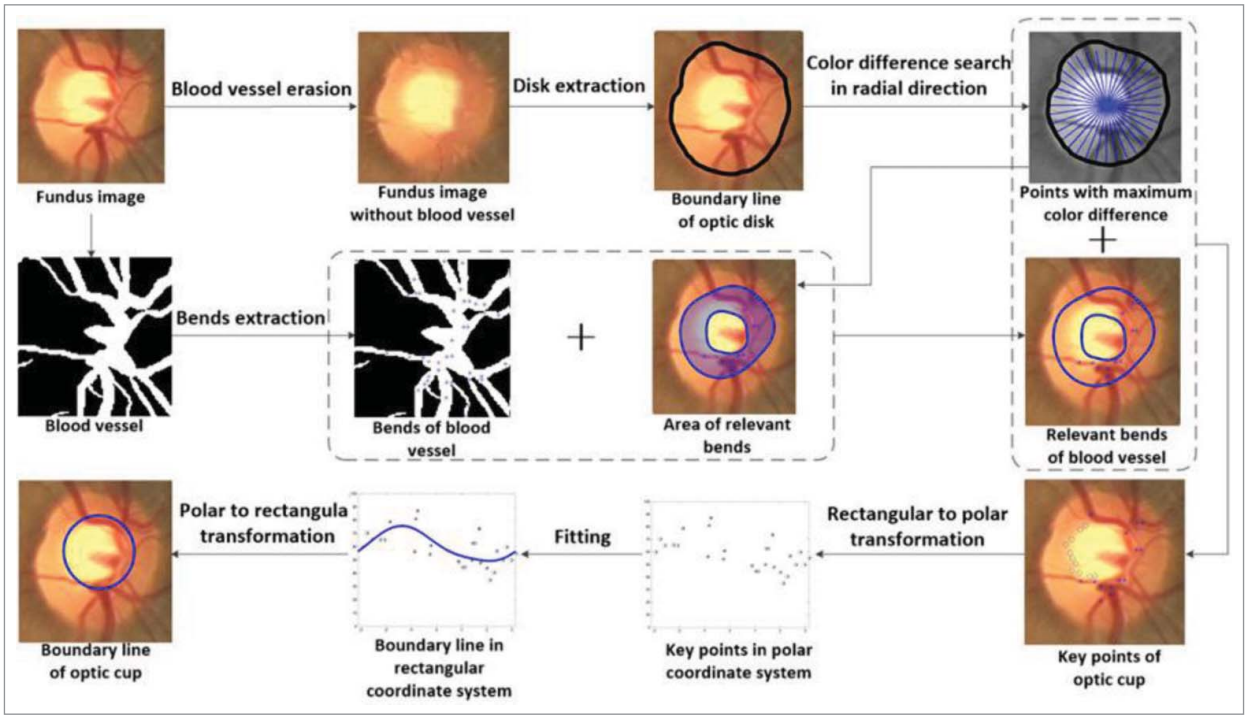


**Figure 2.** Flow Chart of the proposed method.

disc boundary. A ray is drawn from the center of gravity of the disc boundary, and it is rotated every 10 degrees to generate 36 rays. Considering that the optic disc boundary is composed of a set of pixels, in order to determine the center of gravity of the optic disc boundary, its horizontal or vertical coordinate is computed as the average value of the horizontal or vertical coordinates of the pixels. On the segment of each ray located within the disc boundary, one point is taken for every 5 pixels, and the intensity difference between 2 sides of the point along the ray direction from the inner side to the outer side is calculated. In this way, the average intensity values for 5 neighboring pixels at both the inner and outer sides of the target point are calculated along the ray direction, and their difference is recorded.

The point with the maximum intensity difference on each of the 36 rays is defined as the color difference information point. The ratio of the maximum intensity difference on each ray to the average value of all the intensity differences on the same ray is used as the confidence of that information point. The larger the ratio, the more confidence is assigned to the information point. Later, the confidence is used to define the weight of that point in the final cup boundary determination.

Next, a curve fitting method is used to fit the points with maximum intensity differences at 36 directions to a closed curve, which is defined as the initial cup boundary. This boundary is later used to determine the search range for vessel bends. This paper used the regularized fitting method.[24] The advantage of this method is that the complexity of the curve can be defined by adjusting the regularization coefficient. To take advantage of this curve fitting method, the closed curve fitting problem in the original coordinate system is transformed into a curve fitting problem in the polar coordinate system. In other words, the points with maximum intensity differences in a circular area containing the optic disc are transformed from a Cartesian coordinate to a polar coordinate, and they are transformed back after curve fitting. The fitted curve transformed back into the original coordinate is then used as the initial cup boundary.

The next step involves defining the search area for the vessel bends in the vicinity of the initial cup boundary. The confidence of the initial cup boundary is not uniform due to differences in confidence of the information points around the boundary. Therefore, in regions with higher confidence on the initial cup boundary, the color difference information is prioritized, such that the related search area for the vessel bends can be smaller. In contrast, in regions with lower confidence on the initial cup boundary, the vessel bends information should be prioritized, such that

the related search area for the vessel bends should be larger. This study adopted the strategy of setting the local vessel bends search area in the vicinity of the inner and outer sides of the 36 segments of the initial optic cup boundary. In each fundus image, the color difference information point with maximum confidence has maximum search width. The maximum width of the inner search area is set at half of the optic cup radius, and the maximum width of the outer search area is set at 80 percent of the initial rim width. The optic cup radius of some point on the initial optic cup boundary is defined as the distance between this point and the center of gravity of the optic disc; meanwhile, the width of rim at this point is defined as the distance between the point and the corresponding point on the disc boundary. The value of the search width is linear related to the confidence of the color intensity difference. The relevant vessel bends are identified within the search area defined above. In addition to recording the positions of the relevant vessel bends, the bends' curvatures and the vessels' diameters at the corresponding positions are also recorded in order to calculate the confidence of the vessel bends. In general, the greater the curvature, the higher the confidence; the thicker the vessel, the higher the confidence. Therefore, the product of the bend curvature and the corresponding vessel diameter can be used to set the confidence of the vessel bends. This study adopted a dynamic region of support (ROS)-based method to compute the bend points of vessels and the curvatures of these bend points.[25]

Finally, the regularized curve fitting method is used to fit the color difference information points and the vessel bend information points in order to generate the final cup boundary. First, the weight of each information point must be determined. This process includes 2 steps: first, the overall weights of the color difference information points and the vessel bend information points are determined; then, the weight for each type of information points is assigned to each point. In the first step, the minimum weight for the color difference information point is set to 1/3 and the maximum weight is set to 2/3. The weight is linear related to the sum of the confidences of all the color difference information points. In the second step, the weight for color difference information is assigned to each of the 36 color difference information points according to their respective confidences; similarly, the weight for vessel bends information is assigned to each vessel bend according to its respective confidence.

In the end, the weight of each information point is multiplied by 100 and rounded as the number of occurrences of this information point in fitting. The two types of points within the circular area containing the optic disc are transformed from "Cartesian" to "polar" and fitted by the regularized curve fitting method. Finally, the fitted curve obtained is transformed from "polar" to "Cartesian" to generate the fitted curve in the original coordinate system. Thus, the final optic cup boundary is created.

## Experiment

The proposed optic cup segmentation method was evaluated on a public dataset and compared to other optic cup segmentation methods. The results demonstrate that the proposed method has obvious advantages in segmentation accuracy, and the obtained cup boundary is very close to that obtained by ophthalmologists.

### *Experimental design*

The proposed algorithm was evaluated using the public fundus photographs database DRIVE (Digital Retinal Images for Vessel Extraction),[26] and it was then compared to other methods. DRIVE data sets can be downloaded at http://www.isi.uu.nl/Research/Databases, which includes 40 fundus images. In this experiment, 2 ophthalmologists (A and B) were invited to draw the optic cup boundaries. Ophthalmologist A has 10 y of experience in glaucoma diagnosis, and Ophthalmologist B has 5 y of experience in glaucoma diagnosis. The ophthalmologists did not know if the fundus image came from a normal eye or a glaucoma-affected eye. Ophthalmologist A selected 10 fundus images with highest confidence to draw the optic cup boundaries, and the results are used as the standard. Ophthalmologist B's results and other methods were compared to the results from Ophthalmologist A.

The difference of 2 optic cups "A" and "B" drawn by 2 different methods for the same fundus image is defined as $F_{difference} = 1 - \frac{S_{A \cap B}}{S_{A \cup B}}$. Here, $S_{A \cap B}$ represents the intersection area of the optic cups drawn by the 2 different methods, and $S_{A \cup B}$ represents the union area of the optic cups drawn by the 2 different methods. The larger the difference between the 2 drawn boundaries, the greater the value of $F_{difference}$is, and vice versa.

**Table 1.** Values of $F_{difference}$ with Ophthalmologist A for different methods.

| Image number | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Average |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Fitting | 0.68 | 0.61 | 0.19 | 0.53 | 0.43 | 0.47 | 0.77 | 0.48 | 0.38 | 0.21 | 0.48 |
| Interpolation | 0.34 | 0.45 | 0.31 | 0.33 | 0.32 | 0.36 | 0.22 | 0.36 | 0.24 | 0.29 | 0.31 |
| Proposed | 0.18 | 0.45 | 0.22 | 0.20 | 0.14 | 0.17 | 0.20 | 0.14 | 0.26 | 0.12 | 0.22 |

When the 2 boundaries are completely identical, the value of $F_{difference}$ is 0. When the 2 boundaries are completely different, the value of $F_{difference}$ is 1. This experiment used $F_{difference}$ to represent the difference between the cup drawn by the tested method and the cup drawn by Ophthalmologist A. The average value of $F_{difference}$ between the cups drawn by a test method and by Ophthalmologist A for each of the 10 fundus images was used as a reference to evaluate the accuracy of that test method.

### *Experimental results*

The proposed method was compared to 2 classical optic cup segmentation methods. The first is an ellipse fitting method whose basic idea is to identify the closest ellipse to the color difference points as the optic cup boundary. The detailed process is as follows: first, the points with maximum radial color differences are used as information points for fitting; then, the ellipse fitted with regard to these points using the least squares method is taken as the final result. The second classical method is a vessel bends-based interpolation method. The detailed process is as follows: first, the vessel bends points are used as the interpolation information points; then, the Catmull-Rom spline interpolation is used to generate the final result.

Table 1 displays the optic cup segmentation results of the proposed approach and the 2 methods described above. The data in Table 1 indicated that the proposed method achieved a smaller average value of $F_{difference}$ with Ophthalmologist A than the other 2 methods, suggesting that the cup segmentation result obtained by the proposed approach is closer to that obtained by Ophthalmologist A. In addition, the average value of $F_{difference}$ between Ophthalmologists A and

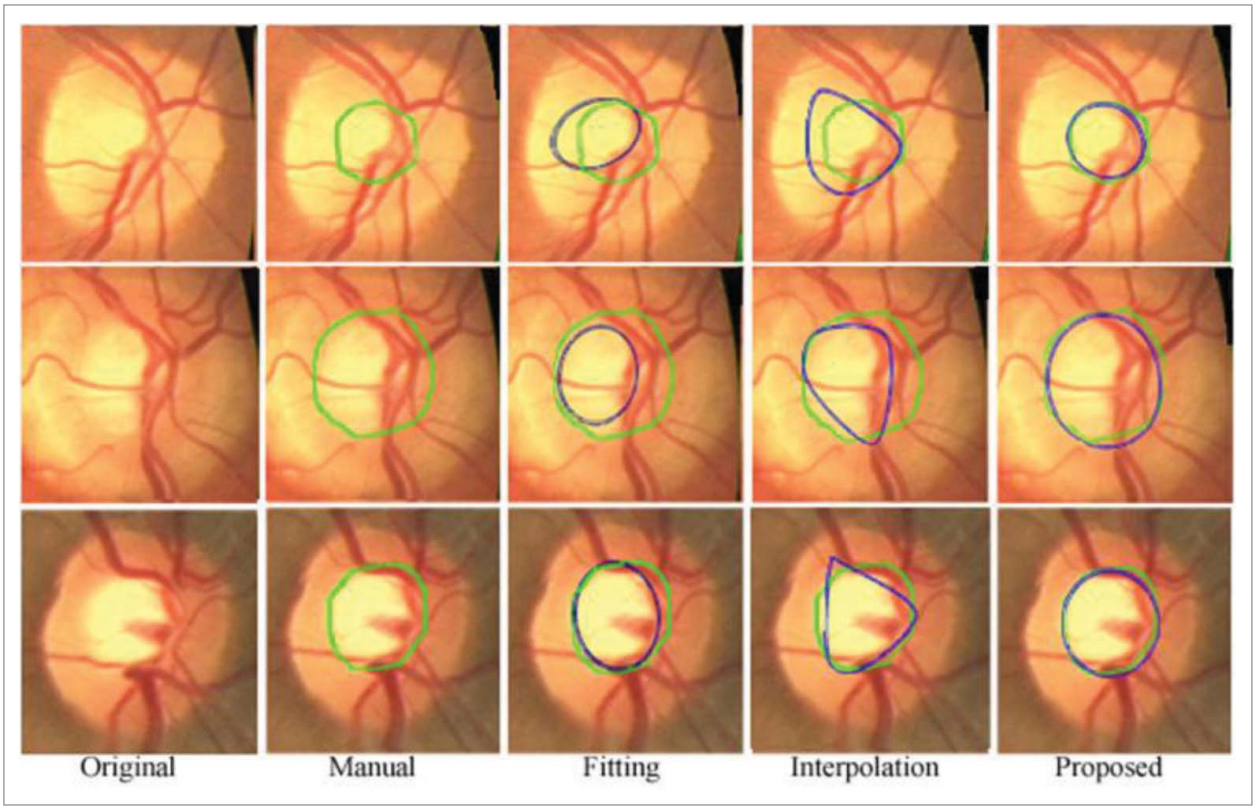


**Figure 3.** Sample results. From left to right columns: the original images, the manual results, the ellipse fitting, the vessel bends interpolation and the proposed method.

B is 0.15. This value can be taken as a reference for evaluating the other methods. As Table 1 shows, the average value of $F_{difference}$ for the proposed method is 0.22, which is only slightly larger than the average value for Ophthalmologist B. This indicates that the difference between the optic cup segmentation result of the proposed method and that of Ophthalmologist A is roughly the same as the difference between the results drawn by the 2 ophthalmologists.

Figure 3 illustrates the optic cup segmentation results from the different methods for 3 typical fundus images. As Fig. 3 shows, the ellipse fitting method worked well for the part of the optic cup with a distinct color difference, but poorly for the part covered by vessels. In contrast, the vessel bends interpolation method extracted a more accurate cup boundary for the part crowded with vessels, with larger errors in the part with sparse vessels. The proposed method simultaneously took advantage of both types of information, allowing it to extract accurate cup boundaries both in areas with high color differences and sparse vessels and in areas with small color differences and crowded vessels.

## Conclusion

This paper proposed an automatic method to extract the optic cup from fundus images. This method takes advantage of both the color difference and the vessel bends simultaneously in order to determine the final cup boundary in a fundus image. During the process of applying both types of information, we learned from the ophthalmologist's strategy by assigning confidence to each information point.

Based on the DRIVE dataset, the proposed method exhibited high consistency with results drawn by ophthalmologists, showing clear advantages over both the ellipse fitting method, which relies only on color information, and the vessel bends interpolation method, which depends only on vessel bends information. Furthermore, the proposed method demonstrated a strong anti-noise effect. In the presence of a small number of inaccurate color information points or vessel bend points, the proposed method can still achieve an accurate optic cup boundary.

## Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

## Funding

This work was supported in part by the National Science Foundation of China, under Grant 11571031 and China Scholarship Council.

## References

[1] Michelson G, Hornegger J, Wärntges S, Lausen B. The papilla as screening parameter for early diagnosis of glaucoma. Dtsch Arztebl Int 2008;105:583-9; PMID:19471619

[2] Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006;90: 262-7; PMID:16488940; http://dx.doi.org/10.1136/bjo.2005.081224

[3] Harizman N, Oliveira C, Chiang A, Tello C, Marmor M, Ritch R, Liebmann JM. The ISNT rule and differentiation of normal from glaucomatous eyes. Arch Ophthalmol 2006;124: 1579-83; PMID:17102005; http://dx.doi.org/10.1001/archopht.124.11.1579

[4] Cheng J, Yin F, Wong DWK, Tao D, Liu J. Sparse dissimilarity-constrained coding for glaucoma screening. IEEE Trans Biomed Eng 2015;62:1395-403; PMID:25585408; http://dx.doi.org/10.1109/TBME.2015.2389234

[5] Xu Y, Jia X, Hu M, Sun X. Feature Extraction from Optic Disc and Cup Boundary Lines in Fundus Images Based on ISNT Rule for Glaucoma Diagnosis. J Med Imaging Health Infor 2015;5: 1833-8; http://dx.doi.org/10.1166/jmihi.2015.1654

[6] Haleem MS, Han L, Hemert JV, Baihua L. Automatic extraction of retinal features from colour retinal images for glaucoma diagnosis: A review. Comput Med Imaging Graph 2013;37: 581-96; PMID:24139134; http://dx.doi.org/10.1016/j.compmedimag.2013.09.005

[7] Miri MS, Abramoff M, Lee K, Niemeijer M, Wang JK, Kwon YH, Garvin MK. Multimodal segmentation of optic disc and cup from SD-OCT and color fundus photographs using a machine-learning graph-based approach. IEEE Trans Med Imaging 2015;34: 1854-66; PMID:25781623; http://dx.doi.org/10.1109/TMI.2015.2412881

[8] Joshi GD, Sivaswamy J, Krishnadas SR. Depth discontinuity-based cup segmentation from multiview color retinal images. IEEE Trans Biomed Eng 2012;59:1523-31; PMID:22333978; http://dx.doi.org/10.1109/TBME.2012.2187293

[9] Stapor K, Sacutewitonski A, Chrastek R, Michelson G. Segmentation of fundus eye images using methods of mathematical morphology for glaucoma diagnosis. International Conference on Computational Science. Springer Berlin Heidelberg, 2004: 41-48.

[10] Inoue N, Yanashima K, Magatani K, Kurihara T. Development of a simple diagnostic method for the glaucoma using ocular fundus pictures. 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference. IEEE, 2006: 3355-3358.

[11] Liu J, Wong D, Lim J, Li H, Tan N, Wong T. Argali—An automatic cup-to-disc ratio measurement system for

glaucoma detection and analysis frame work. SPIE Medical Imaging. International Society for Optics and Photonics, 2009: 72603K-72603K-8.

[12] Joshi GD, Sivaswamy J, Karan K, Krishnadas R. Optic disk and cup boundary detection using regional information. Proceedings of IEEE International Symposium on Biomedical Imaging, 2010 IEEE International Symposium on Biomedical Imaging: From Nano to Macro. IEEE, 2010: 948-951.

[13] Wong DWK, Liu J, Lim JH, Jia X, Li H, Yin F, Wong TY. Level-set based automatic cup-to-disc ratio determination using retinal fundus images in argali. Eng Med Biol Soc 2008;2008:2266-9.

[14] Babu TRG, Shenbagadevi S. Automatic detection of glaucoma using fundus image. Eur J Sci Res 2011;59: 22-32.

[15] Mittapalli PS, Kande GB. Segmentation of optic disk and optic cup from digital fundus images for the assessment of glaucoma. Biomed Signal Proc Control 2016;24, 34-46; http://dx.doi.org/10.1016/j.bspc.2015.09.003

[16] Cheng J, Liu J, Xu Y, Yin F, Wong DWK, Tan NM, Tao D, Cheng CY, Tin A, Wong TY. Superpixel classification based optic disc and optic cup segmentation for glaucoma screening. IEEE Trans Med Imaging 2013;32: 1019-32; PMID: 23434609; http://dx.doi.org/10.1109/TMI.2013.2247770

[17] Xu Y, Duan L, Lin S, Chen X, Wong DWK, Wong TY, Liu J. Optic cup segmentation for glaucoma detection using low-rank superpixel representation. Lecture Notes in Computer Science 2014;17(Pt1):788-95; http://dx.doi.org/10.1007/978-3-319-10404-1_98

[18] Thorat S, Jadhav S. Optic disc and cup segmentation for glaucoma screening based on superpixel classification. Int J Innov Adv Comput Sci 2015;4:167-72.

[19] Wong DWK, Liu J, Lim JH, Li H, Wong TY. Automated detection of kinks from blood vessels for optic cup segmentation in retinal images. SPIE Medical Imaging. International Society for Optics and Photonics, 2009: 72601J-72601J-8.SPIE Medical Imaging. International Society for Optics and Photonics, 2009: 72601J-72601J-8.

[20] Joshi GD, Sivaswamy J, Krishnadas SR. Optic disk and cup segmentation from monocular color retinal images for glaucoma assessment. IEEE Trans Med Imaging 2011;30: 1192-205; PMID:21536531; http://dx.doi.org/10.1109/TMI.2011.2106509

[21] Hatanaka Y, Nagahata Y, Muramatsu C, Okumura S, Ogohara K, Sawada A, Ishida K, Yamamoto T, Fujita H. Improved Automated Optic Cup Segmentation Based on Detection of Blood Vessel Bends in Retinal Fundus Images, Improved automated optic cup segmentation based on detection of blood vessel bends in retinal fundus images. International Conference of the IEEE Engineering in Medicine & Biology Society. IEEE 2014:126-129.

[22] Fraz MM, Remagnino P, Hoppe A, Uyyanonvara B, Rudnicka AR, Owen CG, Barman SA. Blood vessel segmentation methodologies in retinal images–a survey. Comput Methods and Programs Biomed 2012;108: 407-33; http://dx.doi.org/10.1016/j.cmpb.2012.03.009

[23] Mendonça AM, Campilho A. Segmentation of Retinal Blood Vessels by Combining the Detection of Centerlines and Morphological Reconstruction. IEEE Trans Med Imaging 2016;25: 1200-13; http://dx.doi.org/10.1109/TMI.2006.879955

[24] Ramsay JO, Silverman BW. Applied Functional Data Analysis: Methods and case Studies, New York: Springer, Inc. 2002.

[25] He XC, Yung NHC. Curvature scale space corner detector with adaptive threshold and dynamic region of support, inInt. Conf. Pattern Recogni, 2004, pp. 791-794.

[26] Niemeijer M, Staal J, van Ginneken B, Loog M, Abramoff MD. Comparative study of retinal vessel segmentation methods on a new publicly available database. Proceedings of SPIE-The International Society for Optical Engineering 2004:648-656.