Automated identification of retinal vessels using a multiscale directional contrast quantification (MDCQ) strategy

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Purpose: A novel algorithm is presented to automatically identify the retinal vessels depicted in color fundus photographs.

Methods: The proposed algorithm quantifies the contrast of each pixel in retinal images at multiple scales and fuses the resulting consequent contrast images in a progressive manner by leveraging their spatial difference and continuity. The multiscale strategy is to deal with the variety of retinal vessels in width, intensity, resolution, and orientation; and the progressive fusion is to combine consequent images and meanwhile avoid a sudden fusion of image noise and/or artifacts in space. To quantitatively assess the performance of the algorithm, we tested it on three publicly available databases, namely, DRIVE, STARE, and HRF. The agreement between the computer results and the manual delineation in these databases were quantified by computing their overlapping in both area and length (centerline). The measures include sensitivity, specificity, and accuracy.

Results: For the DRIVE database, the sensitivities in identifying vessels in area and length were around 90% and 70%, respectively, the accuracy in pixel classification was around 99%, and the precisions in terms of both area and length were around 94%. For the STARE database, the sensitivities in identifying vessels were around 90% in area and 70% in length, and the accuracy in pixel classification was around 97%. For the HRF database, the sensitivities in identifying vessels were around 92% in area and 83% in length for the healthy subgroup, around 92% in area and 75% in length for the glaucomatous subgroup, around 91% in area and 73% in length for the diabetic retinopathy subgroup. For all three subgroups, the accuracy was around 98%.

Conclusions: The experimental results demonstrate that the developed algorithm is capable of identifying retinal vessels depicted in color fundus photographs in a relatively reliable manner.

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Key words: fundus photograph, retinal vessels, segmentation, multiscale quantification

1. INTRODUCTION

As the sole part of the central nervous system (CNS) that can be noninvasively visualized using optic techniques (e.g., color retinal photography), the retina is responsible for reconstructing the images of the external world for human brains in real time.¹ To provide adequate energy for this “image reconstruction” processing, a unique network of blood vessels is formed on the retina. Any abnormality affecting the delivering capability of retinal vessels may result in malfunction

of the eyes (e.g., impaired vision). In addition, a large variety of systematic diseases (e.g., diabetes, hypertension, arteriosclerosis, cardiovascular diseases, and stroke) and retinal diseases (e.g., retinopathy of prematurity, glaucoma, and maculopathy) are closely associated with retinal vessels.^{2–6} Accurate quantification of the morphological properties of retinal vessels, such as diameter, length, branching angle, and tortuosity, as well as their abnormalities or variations over time, may improve the diagnosis performance (e.g., accuracy and efficiency) of ophthalmologists.^{7–9} In clinical practice, color

FIG. 1. Schematic flowchart of the retinal vessel identification algorithm.

retinal photography is widely used as an essential tool for diagnosis of various eye diseases. However, given the large number of vessels depicted in a single fundus image, it is very time-consuming for human experts to manually trace the vessels, not to mention the unavoidable large inter- and/or intrareader variability.¹⁰ Hence, it is extremely desirable to have a computer tool to aid in an efficient and objective quantification of vessel morphology.¹¹ A prerequisite for this purpose is to accurately delineate the boundary of retinal vessels.

In the past, there have been a large number of computer algorithms developed to automatically segment the vessels depicted in retinal fundus photographs.^{12–39} Various characteristics of vessels and images were explored, including but not limited to color, intensity, shape, gradient, contrast, and connectivity as well as relevant anatomy knowledge. Even though, it remains a challenging task to reliably and accurately delineate (small) vessels in particular in the presence of diseases (e.g., severe hemorrhage). The primary challenge is the large variability of fundus images in appearance (e.g., low contrast and luminosity) and the diversity of individuals in biology or anatomy.⁴⁰ Even for the same image acquired on the same subject, the appearance of retinal vessels may vary when they are located at different regions of the image. These issues could be amplified in the presence of severe retinal diseases. In methodology, available approaches could be roughly classified into four broad categories: (1) line or edge tracing,^{12–20} (2) multiscale filtering,^{21–27} (3) morphological deformation,^{28–32} and (4) machine learning based classification.^{32–38} By exploiting the linear structure of retinal vessels, the line or edge tracing method typically identifies a set of initial seed points and then starts from them to progressively trace the vessels. Since retinal vessels vary in width, intensity, and orientation, the multiscale filtering method detects the vessels in a progressive manner at different scales of specific measures, such as angles, gradients, and thresholds, to capture the local changes of the vessels in terms of these measures. The machine learning based classification method defines a number of domain rules or image features at the level of individual pixels and then classifies each pixel into either vessel or nonvessel using a training or machine learning procedure (e.g., neural network or support vector machine). Detailed descriptions of available approaches as well as their performance can be found in a survey.⁴⁰

In this study, we present a fully automated retinal vessel segmentation algorithm termed multiscale directional contrast quantification (MDCQ). The underlying idea is to explore the linear structure of retinal vessels by quantifying the local contrast of each pixel as compared with its background at multiple scales as a way for vessel enhancement and then fuse the identified consequent contrast images to identify the final vessels with noisy alleviation. The contrast quantification procedure serves as an image intensity normalization in nature. The performance of the developed scheme was quantitatively as-

sessed using three publicly available databases with human manual delineations.

2. METHODS

2.A. Scheme overview

As illustrated in Fig. 1, the proposed algorithm consists of three steps. Similar to previous investigations,^{12–39} the first step is to extract the green channel from a color retinal fundus photograph in RGB format, because this channel provides the highest contrast between vessels and background. Thereafter, a MDCQ strategy is used to transform the green channel image into a contrast image, where the value of each pixel denotes its contrast with the local surrounding regions. As a vessel enhancement procedure, this strategy overcomes the variability of vessels in appearance (i.e., intensity and size) at different locations of a fundus image. Third, a differential fusion strategy is used to combine the results identified at different scales and meanwhile remove noisy regions. Finally, the missing of vessels caused by central light reflex is fixed by conducting a simple filling operation. A detailed description of these steps and their implementation is presented in Secs. 2.B–2.E.

2.B. Multiscale directional contrast quantification

As the name implies, the MDCQ strategy aims to quantify the contrast of each pixel in a retinal image from two aspects: (1) “multiscale” and (2) “directional.” The “multiscale” is to deal with the variety of retinal vessels in width or size and in image resolution, and the “directional” is to handle the variety of retinal vessels in orientation. The contrast quantification serves as an image transformation or a normalization procedure to alleviate the variety of retinal vessels in intensity. Here, we defined the contrast at a given pixel as the maximum difference in averaged intensity between this pixel and the neighboring line segments among all directions, i.e.,

$$T(i, j) = \max \left\{ t_\theta = \frac{1}{d} \sum_{k=1}^d I_k^\theta - I(i, j), \theta \in [0, 2\pi] \right\}, \quad (1)$$

where d is the length of a line segment and varies within certain value depending on the largest width of retinal vessels, and I^θ is the intensity of a given pixel along a specified direction. We note that $T(i, j)$ will be negative when the pixel has a higher intensity than its background. Because retinal vessels always have a lower intensity as compared to its local background, the maximum positive value of $T(i, j)$ is used as the contrast of the pixel at (i, j) . Given the “elongated” structures of retinal vessels, this contrast definition actually aims to capture the gradient of the image along the “width” direction [Fig. 2(a)]. Unlike traditional methods (e.g.,

FIG. 2. Illustration of the concepts involved in the MDCQ strategy: (a) the “width” and “elongated” directions of a vessel, (b) eight equally distributed directions, and (c) neighboring line segments at point p_i .

structure tensor⁴¹) that define the gradients as the difference between the intensities of two neighboring pixels, we compute the contrast as the difference between the pixels and the intensities of their neighboring line segments. The “average” strategy in Eq. (1) has a smoothing characteristics and could largely alleviate the impact of image noises or artifacts. Since the orientations and the widths of retinal vessels vary in the fundus image space, we used a “multiscale” direction and a “multiscale” distance. In implementation, eight equally distributed directions [Fig. 2(b)] are used, and the length of a line segment d [Fig. 2(c)] varies dynamically (e.g., ranging 1–50 pixels) to capture different sizes of vessel, depending on image resolution or vessel width in terms of pixel. Whereas the size of vessels (unit: pixels) varies when the image resolution is different, determining the value of d needs the consideration of image resolution as well.

Application of the above described transformation will convert the original green-channel image into a contrast image, which is a gray-scale image. The value of each pixel in the contrast image is the contrast of the pixel. Because the vessels have a relatively higher contrast as compared to their surrounding background (e.g., the examples in Fig. 3), the regions with a relatively large value in the contrast images tend to be vessels. The examples in Fig. 3 show the appearances of the transformed images when using different values of d . It can be seen from these contrast images that small vessels are enhanced. Typically, as demonstrated by the local enlargements in Fig. 4, larger values of d have less noisy regions but may miss small vessels. When retinal images have different resolutions and/or different image qualities, it is difficult to adaptively determine the optimal value of d . Hence, given the contrast images obtained at different scales, it is desirable to find a fusion solution that could combine their complementary merits properly and thus largely remove the image noisy regions while maintaining a high sensitivity in identifying vessels.

2.C. Differential fusion

Considering the random characteristic of image noise and/or artifacts in space, we propose to combine the images

obtained at different d in a progressive manner using a differential fusion approach. The flowchart in Fig. 5 and the example in Fig. 6 are used to aid the explanation of the differential fusion procedure.

Step (1): Obtain an initial contrast image at a large d_0 value and denote it as R_0 . The reason that the fusion starts from the contrast image obtained at a large d value is that such an image has less noisy regions. For example, the contrast image in Fig. 6(a) is obtained at a d value of 30 pixels.

Step (2): Decrease the d_0 value at a fixed step Δd and compute the contrast image at this value. The resulting image is denoted as R_i . To clearly demonstrate the difference between R_0 and R_i , we used an image obtained at a relatively small d value of five pixels, as shown in Fig. 6(b).

Step (3): Compute the average image U_i and the overlapping image D_i between R_0 and R_i . U_i is a grayscale image. The pixel value of U_i is the averaged contrast of R_0 and R_i at the same location. D_i is a binary image. When R_0 and R_i overlap at a specific location, the pixel value of D_i is “1”; otherwise, the pixel value is “0.” Due to its “differential” characteristic, D_i contains a large number of small regions formed by connected pixels. The images in Figs. 6(c) and 6(d) show the overlapping image D_i and the average image U_i , respectively.

Step (4): Identify isolated small clusters in D_i and remove those that do not appear as an elongated shape as well as their correspondences in U_i . Here, an isolated cluster is a region formed by a list of pixels that are eight-connected in image space. We quantify the elongation as $L = \frac{S^2}{V}$, where S is the longest distance of a clustered region, and V is the area of this clustered region. A higher value means a more elongated shape. Removing the noisy nonelongated regions will result in a relatively “clean” image, and we assign it to R_0 . The underlying idea of this step is that the overlapping regions between two consequent images obtained at different d values tend to be vessels, because these regions have a contrast as compared with surrounding areas at different values of d ; otherwise, they may be not. The example in Fig. 6(e) shows the fused image between the images in Figs. 6(a) and 6(b). In fact, most of the regions in Fig. 6(c) were discarded as noise from the union of the images in Figs. 6(a) and 6(b). As a result, a relatively “clean” image is obtained.

FIG. 3. Examples demonstrating the transformed results (i.e., contrast image) when using different d .

Step (5): Repeat Steps (2)–(4) until the d_0 is equal to one pixel. The goal of the progressive fusion strategy is to repeatedly identify the overlapping regions as vessels, while discard the nonoverlapping and nonlinear regions as nonvessels.

Step (6): Remove the small isolated clusters in the final U_i . The image in Fig. 6(f) shows the identified vessels when

only the images in Figs. 6(a) and 6(b) are used. The image in Fig. 6(g) shows the identified vessels when d decreased progressively from 30 pixels to 5 pixels at an interval of 5 pixels.

In the above procedure, d_0 could be initially set at the largest width of retinal vessels. For Δd , a simple way is to set it at a single pixel, but this may result in a large number of

FIG. 4. Illustration of the impact of d on vessel identification. (a) and (b) show the local enlargements of the regions indicated by the boxes in Figs. 3(1-a) and 3(1-d), respectively, and (c) and (d) show the local enlargements of the regions indicated by the boxes in Figs. 3(2-a) and 3(2-d), respectively. The arrows indicate some small vessels.

FIG. 5. The flowchart of the differential fusion procedure.

iterations and thus lead to a high computational cost. Hence, it is prudent to determine Δd according to the resolution of the original fundus image. In our implementation, we empirically set Δd at $\text{MAX}(\text{image resolution}/1000, 1)$. When removing noisy nonvessel (nonelongated) regions, we uniformly set a threshold of 5, which means that the length of a shape is five times its width. We note that the “progressive” characteristic of the above fusion process is to avoid the fusion of the noisy regions in space. In other words, the vessels are fused progressively and meanwhile the noisy regions (e.g., the macula region in Fig. 6) are discarded progressively. As the image in Fig. 6(f) demonstrates, when the interval value (i.e., 25 pixels) is large, some noisy regions may be fused. In contrast, as the image in Fig. 6(g) shows, when the interval value (i.e., five pixels) is small, there is almost no noisy region. This is attributed to the progressive differential fusion procedure.

2.D. Central light reflex region filling

In the presence of obvious central light reflex in arteries/veins, the contrast in the inner parts of the vessels after the application of the MDCQ procedure may be lower, albeit their absolute intensities are high. As a result, the inner parts of the vessels may not be well depicted in the contrast image as compared to the edges of the vessels [Fig. 7(b)]. To fill these missed central light reflex regions, a straightforward solution is to perform a “closing” morphological operation. However, this procedure may fuse the neighboring vessels when the kernel size is not properly set. Hence, we propose a simple scanning line approach. As shown by the example in Fig. 7(b), a line scans the image vertically and horizontally and small gaps (in orange) less than the width of the vessels are filled as vessels. The example in Fig. 7(c) shows the filled regions.

2.E. Performance validation

Like most available retinal vessel segmentation algorithms, the performance of the developed algorithm was assessed using two publicly available databases, namely, DRIVE (Digital Retinal Images for Vessel Extraction: <http://www.isi.uu.nl/Research/Databases/DRIVE/>) (Ref. 13) and STARE (STructured Analysis of the Retina: <http://www.ces.clemson.edu/~ahoover/stare/>).²² The DRIVE database contains a total of 40 color fundus photographs acquired using a Cannon CR5 nonmydriatic 3-CCD camera, among which 20 photographs were designed for testing purpose and the other 20 for training purpose. The field of view (FOV) is around 550×550 pixels. For the 20 testing images, two observers were asked to manually delineate the boundary of the depicted retinal vessels. The STARE database is composed of 20 fundus photographs acquired using a TopCon TRV-50 fundus camera, among which there were ten pathological cases. The FOV is approximately 650×550 pixels. Similar to the DRIVE, two observers manually segmented all the vessels depicted on these images. We note that the DRIVE database provides the mask of the FOV, while the STARE database does not. Considering that the image resolution of the fundus photographs in the DRIVE database and the STARE database is relatively low, we also tested our algorithm on a third publicly available database called HRF (High-Resolution Fundus: <http://www5.cs.fau.de/research/data/fundus-images>) database,⁴² which contained 45 high resolution fundus photographs and were acquired on 15 healthy patients, 15 glaucomatous patients, and 15 diabetic retinopathy patients separately using a Canon CR-1 fundus camera. The FOV is approximately 3500×2500 pixels. Detailed descriptions of the three databases can be found in Refs. 13, 22, and 42. It is notable that we did not use any of the cases in these databases but our own cases (i.e., collected from National Engineering Research Center for Ophthalmic Equipments, Beijing Tongren Hospital, Beijing, P. R. China) for the development purpose. All cases in these public databases were used purely for the validation purpose.

When assessing the difference between the computer results and the manual segmentation results in the above three databases, we computed three measures, namely accuracy, sensitivity (or recall), and precision, from both area and length (centerline) perspectives. The area perspective considers the area overlapping between two segmentation results, while the length perspective considers the centerline overlapping between two segmentation results. The accuracy is defined by the ratio between the correctly classified pixels (including vessels and nonvessels) and the total pixels in the FOV (the DRIVE and HRF databases where the FOV masks are available) or the whole image (the STARE database where the FOV mask is not available). For the skeleton-based assessment, we do not provide the accuracy measure, because skeletons have only a pixel-width and this will typically cause a very high accuracy measure. The sensitivity (or recall) is measured by the ratio between the correctly identified pixel number and the manually identified pixel number, reflecting how

FIG. 6. Illustration of the differential fusion strategy. (a) $d = \text{pixel}$; (b) $d = 5 \text{ pixel}$; (c) difference image D_i between (a) and (b); (d) union image U_i between (a) and (b); (e) fused image; (f) small cluster removal and (g) identified vessels when d decreased progressively from 30 pixels to 5 pixels at an interval of 5 pixels.

much the vessels are correctly identified. The precision is defined as the ratio between correctly identified pixel number and the total identified pixel number, reflecting the level of over-segmentation.

Considering that the manual segmentation may not delineate the boundaries of retinal vessels with an accuracy of 100%, we allowed a tolerance when deciding whether a pixel was correctly identified as part of the vessels. In other words, if a pixel is close to the manual results within a certain range or error (unit: pixels), we assume that the pixel is located on retinal vessels. In a study that focused specifically on quantitative evaluation of a retinal blood vessel segmentation scheme, Nguyen *et al.* emphasized that small localiza-

tion errors were typically unavoidable in a segmented image and the introduction of a tolerance would not affect the desired retinal features.⁴³ We presented the results separately when the tolerance varied, depending on the image resolution. Specifically, for the DRIVE and STARE databases, the tolerance ranged from zero to three pixels; while for the HFR database, the tolerance ranged from zero to ten pixels. Given the fixed physical dimension of an eye, there will be more pixels when the pixel's size is smaller or the resolution is higher. As a result, a larger pixel tolerance is allowed for high resolution images. An experiment was performed on the HFR dataset to assessing the impact of tolerance on performance assessment.

FIG. 7. Filling the central light reflex regions using horizontal and vertical scanning lines. (a) shows the local enlargement of the original image indicated by the box in Fig. 6(g), (b) shows the region in (a) before the central light reflex regions were filled, and (c) shows the result after the gaps (indicated by the arrows) formed by the central light reflex regions in (b) were filled.

In addition, unlike traditional methods, we applied a skeletonization procedure to the manual segmentation results in the above databases and the computer segmentation results. The purpose is to identify the skeletons or centerlines of the vessels and compute their agreement. When computing the agreement between the skeletons, we allowed a tolerance as well, because local image noise may lead to somewhat perturbation of the centerlines. We also computed the average distance between the centerlines of the manual segmentation

results and the centerlines of the computer results. The distance is defined as the shortest distances from every point from one centerline to the other centerline and vice versa. Extracting centerlines or skeletonization has been widely investigated in the area of computer graphics. Here, we used a general skeletonization algorithm developed by Cornea *et al.*⁴³ The example in Fig. 8 shows the results after the application of this skeletonization algorithm to retinal vessels, where different branches are encoded with different colors. Finally,

FIG. 8. The left images in (a) and (b) show the vessels manually delineated by human experts, and the right images show the centerlines identify by the skeletonization algorithm developed by Cornea *et al.* (Ref. 43). (a) the first image in the DRIVE testing database and (b) the first image in the STARE testing database.

TABLE I. Performance measures (%) of the proposed method on the DRIVE database.

Observer	Tolerance (unit: pixel)	Area			Skeleton	
		Sensitivity (unit:%)	Precision (unit:%)	Accuracy (unit:%)	Sensitivity (unit:%)	Precision (unit:%)
1	0	67.30 ± 4.78	66.33 ± 4.78	91.43 ± 0.83	30.38 ± 4.45	37.30 ± 3.11
	1	84.65 ± 3.51	88.99 ± 3.42	97.85 ± 0.54	69.79 ± 6.91	83.66 ± 3.38
	2	87.60 ± 3.01	92.41 ± 3.20	98.70 ± 0.46	73.90 ± 6.63	90.48 ± 3.13
	3	90.19 ± 2.60	94.97 ± 3.07	99.28 ± 0.42	77.18 ± 6.27	93.65 ± 3.09
2	0	69.62 ± 3.51	66.04 ± 5.02	91.86 ± 0.62	32.17 ± 3.77	37.93 ± 2.07
	1	86.43 ± 3.60	89.03 ± 3.79	98.05 ± 0.48	72.30 ± 5.52	84.88 ± 2.33
	2	88.93 ± 3.49	92.27 ± 3.60	98.78 ± 0.47	76.35 ± 5.45	89.49 ± 2.44
	3	91.11 ± 3.25	94.86 ± 3.39	99.29 ± 0.46	79.73 ± 5.24	92.78 ± 2.49

the computational cost of the segmentation procedure was reported.

3. RESULTS

3.A. Testing on the DRIVE database

The performance measures on the DRIVE database were listed in Table I. When compared with the two observers' manual results, the sensitivities in identifying vessels in area and length were around 90% and 77%, respectively, the accuracy in pixel classification was around 99%, and the precisions in terms of both area and length were around 94%. The average distance between the computer results and the manual delineations was summarized in Table II. When the manual segmentation results by Observer #2 was regarded as the reference standard, the average distance from the centerlines of the computer results to the manual results is smaller than the average distance from the results by Observer #1 to the results by Observer #2. The examples in Fig. 9 show the best and the worst segmentation results by the computer algorithm and the manual segmentation results by the two observers.

TABLE II. The average distances (unit: pixel) between the centerlines of the manual segmentation results and the centerlines of the computer segmentation results. (In the HRF database, the manual segmentation results were obtained by only one observer.)

Database	Category	Average distance (from A to B)	Average distance (from B to A)
DRIVE	A: Computer result B: Observer #1	1.27 ± 0.43	3.64 ± 1.04
	A: Computer result B: Observer #2	1.34 ± 0.40	3.18 ± 0.80
	A: Observer #1 B: Observer #2	1.61 ± 0.59	1.24 ± 0.47
	A: Computer result B: Observer #1	3.19 ± 1.61	2.36 ± 0.96
STARE	A: Computer result B: Observer #2	1.50 ± 0.69	5.65 ± 1.77
	A: Observer #1 B: Observer #2	0.79 ± 0.37	5.94 ± 1.79
	A: Computer result B: Observer #1	3.78 ± 0.97	7.69 ± 2.80
	A: Computer result B: Observer #2	2.84 ± 0.57	11.40 ± 1.68
HRF	Healthy	4.45 ± 2.35	11.61 ± 3.34
	Glaucomatous		
	Diabetic retinopathy		

The computational cost for identifying the retinal vessels in the DRIVE database was around 2 s per case on a desktop PC (AMD Athlon™ 64 × 2 Dual 2.11 GHZ CPU and 8 GB RAM).

3.B. Testing on the STARE database

The performance measures on the STARE database were listed in Table III. When compared with the two observers' manual results with a tolerance of three pixels, the sensitivities in identifying vessels were around 90% in area and 70% in length, and the accuracy in pixel classification was around 97%. For the first observer, the precisions in terms of both area and length were around 85%; while for the second observer, the precisions in terms of both area and length were around 93%. The average distance between the computer results and the manual delineations was summarized in Table II. The examples in Fig. 10 show the best and the worst segmentation results by the computer algorithm and the manual segmentation results by the two observers in the database. The computational cost for the cases in the STARE database is similar to that for the DRIVE database.

3.C. Testing on the HRF database

The performance measures on the HRF database were listed in Table IV. When compared with the observer's manual results with a tolerance of six pixels, the sensitivities in identifying vessels were around 92% in area and 83% in length for the healthy subgroup, around 92% in area and 75% in length for the glaucomatous subgroup, around 91% in area and 73% in length for the diabetic retinopathy subgroup. For all three subgroups, the accuracy was around 98%. The average distance between the computer results and the manual delineations was summarized in Table II. The examples in Fig. 11 show the best and the worst segmentation results by the computer algorithm as well as their corresponding manual segmentation results. The computational cost for identifying the retinal vessels in the HRF database was around 110 s per case on a desktop PC (AMD Athlon™ 64 × 2 Dual 2.11 GHZ CPU and 8 GB RAM).

3.D. Impact of tolerance on performance assessment

When the tolerance was different, the performance measures on the HRF database, including sensitivity, precision,

FIG. 9. Two examples showing the images with the best (i.e., Case #1 in the top row) and the worst (i.e., Case #7 in the bottom row) segmentations after the application of the algorithm to the DRIVE database: (a) the origin fundus images, (b) the manual segmentation results by Observer #1, (c) the manual segmentation results by Observer #2, and (d) the computer results.

and accuracy, were listed in Fig. 12. When the tolerance is zero, the sensitivity is around 82%, the precision varies from 60% to 71% for different subgroups, and the sensitivity is around 95%. It can be seen that the performance varies slightly if the tolerance is larger than six pixels. This is relatively small as compared with the resolution of the fundus images (i.e., 3500×2500 pixels).

4. DISCUSSION

We described a novel scheme termed MDCQ to automatically identify retinal vessels depicted in color fundus photographs. This scheme deals with the variety of retinal vessels in intensity, width, and orientation using a multiscale strategy. Its novelty lies primarily in two aspects: (1) enhancing vessels by transforming a fundus image into a contrast image, (2) differential fusion of transformed images obtained at multiple scales in a progressive manner. The local contrast quantification procedure serves as an image intensity normal-

ization in nature and thus overcome the variety of retinal vessels in intensity regardless of their size (width), location, and image resolution (Fig. 3). The differential fusion procedure provides a mechanism that combines the results obtained at multiple scales and meanwhile alleviates image noises and/or artifacts by leveraging the difference and the spatial continuity between consequent contrast images (Fig. 6). In addition, this scheme is easy to implement and does not involve any training procedure that typically requires a large amount of diverse prelabeled data and/or prior domain knowledge or rules. The performance of the developed scheme was assessed using three different publicly available databases, which were acquired on both healthy and diseased subjects using different cameras and include both low and high resolution images. Our experimental results demonstrate the reliability of this scheme in identifying small retinal vessels.

The usage of publicly available databases makes it possible to conduct a direct comparison with other approaches. In a recent survey, Fraz *et al.* conducted a relatively comprehensive

TABLE III. Performance measures (%) of the proposed method on the STARE database.

Observer	Tolerance (unit: pixel)	Area			Skeleton	
		Sensitivity (unit:%)	Precision (unit:%)	Accuracy (unit:%)	Sensitivity (unit:%)	Precision (unit:%)
1	0	68.80 ± 6.68	63.21 ± 7.80	94.43 ± 1.16	36.07 ± 3.82	35.12 ± 4.40
	1	86.18 ± 6.07	80.71 ± 7.40	95.82 ± 0.86	80.19 ± 5.46	77.80 ± 7.09
	2	89.14 ± 5.48	83.44 ± 7.43	96.34 ± 0.82	84.30 ± 5.12	81.82 ± 7.03
	3	91.60 ± 4.75	86.04 ± 7.21	96.79 ± 0.77	87.31 ± 4.79	84.80 ± 6.76
2	0	56.56 ± 6.00	72.73 ± 9.80	92.92 ± 1.54	24.86 ± 3.30	35.54 ± 4.45
	1	74.25 ± 6.20	89.02 ± 8.41	95.85 ± 0.85	57.89 ± 6.47	82.07 ± 6.71
	2	78.36 ± 5.98	91.55 ± 7.30	96.60 ± 7.31	62.25 ± 6.64	87.64 ± 5.90
	3	82.42 ± 5.56	94.12 ± 5.92	97.31 ± 0.57	66.40 ± 6.66	92.15 ± 4.91

FIG. 10. Two examples showing the images with the best (i.e., Case #5 in the top row) and the worst (i.e., Case #13 in the bottom row) segmentations after the application of the algorithm to the STARE database: (a) the origin fundus images, (b) the manual segmentation results by Observer #1, (c) the manual segmentation results by Observer #2, and (d) the computer results.

investigation of available retinal vessel segmentation approaches and summarized their performance in a set of tables.⁴⁰ Most of these approaches were assessed using the STARE and/or the DRIVE databases. As a supervised method known as the feature-based AdaBoost classifier (FABC), the algorithm developed by Lupascu *et al.* has the best performance with an accuracy of 95.9% and a sensitivity of 72% for the DRIVE database to date.³⁴ In contrast, our algorithm does not involve any machine learning procedure and has an accuracy of around 99% and a sensitivity of 90% for the same database when a tolerance of three pixels is allowed. When comparing with the manual results in the high-resolution HRF database, the approach developed by Odstreilik *et al.* achieved an accuracy of around 95% and a sensitivity of ranging from 74% to 79% for the three subgroups;⁴² in contrast, our approach has an accuracy of around 98% and a sensitivity of 90% when a tolerance of 10 pixels is allowed. Despite its

relatively high performance as compared with available approaches, we are aware that this scheme still missed some small vessels and introduced some false positives in particular in the presence of diseases or severe image noise/artifacts (Figs. 9–11). It is notable that we used a tolerance when comparing with the manual delineations in these databases. This may present an “unfair” comparison; however, we agree with Nguyen *et al.* that this “tolerance” could affect the segmented retinal features obviously.⁴³ In particular, we believe that it is reasonable to use a tolerance when comparing with manual results. As the cases in the DRIVE and the STARE databases showed, a large portion of small vessels have a width of a single or two pixels; hence, it is very difficult to exactly match the manual segmentation results at the small airways if there is no tolerance. As demonstrated by the results in Table II, for the DRIVE database, the average centerline distances between the manual results by two observers are even larger than

TABLE IV. Performance measures (%) of the proposed method on the HRF database.

Subgroup observer	Tolerance (unit: pixel)	Area			Skeleton	
		Sensitivity (unit:%)	Precision (unit:%)	Accuracy (unit:%)	Sensitivity (unit:%)	Precision (unit:%)
Healthy	0	81.76 ± 3.86	75.72 ± 2.78	95.10 ± 0.59	24.41 ± 3.57	27.98 ± 2.43
	2	89.69 ± 3.04	86.28 ± 2.51	97.59 ± 0.42	67.49 ± 6.84	76.16 ± 3.51
	4	92.07 ± 2.60	91.18 ± 2.31	98.57 ± 0.31	78.41 ± 5.87	88.03 ± 2.35
	6	92.79 ± 2.46	93.40 ± 2.15	98.81 ± 0.26	81.80 ± 5.61	91.29 ± 2.23
Glaucomatous	0	83.02 ± 2.45	63.57 ± 3.00	94.71 ± 0.66	16.67 ± 1.73	21.83 ± 2.12
	2	88.84 ± 1.83	80.51 ± 2.65	97.50 ± 0.44	54.25 ± 3.67	69.37 ± 3.90
	4	90.79 ± 1.51	90.02 ± 2.20	98.63 ± 0.32	69.80 ± 2.99	88.26 ± 2.38
	6	91.51 ± 1.37	94.17 ± 1.8	98.99 ± 0.25	74.72 ± 2.57	93.58 ± 1.63
Diabetic retinopathy	0	81.20 ± 4.73	59.58 ± 4.90	93.92 ± 0.84	14.80 ± 2.09	18.99 ± 2.09
	2	87.02 ± 4.15	75.67 ± 5.01	96.68 ± 0.67	49.49 ± 4.82	61.99 ± 3.63
	4	89.44 ± 3.82	85.72 ± 4.58	98.01 ± 0.58	66.55 ± 5.39	82.34 ± 4.96
	6	90.52 ± 3.60	90.81 ± 4.06	98.55 ± 0.50	72.96 ± 5.75	89.39 ± 4.03

FIG. 11. Two examples showing the images with the best (i.e., top row: Case #15 in the healthy subgroup) and the worst (i.e., bottom row: Case #14 in the glaucomatous subgroup) segmentations after the application of the algorithm to the HRF database: (a) the origin fundus images, (b) the manual segmentation results, and (c) the computer results.

FIG. 12. (a)–(c) Illustration of the impact of the tolerance on the performance validation using the HRF database.

the average centerline distance from the computer results to the manual delineation. Assume that the vessels appear as a linear shape and the widths of the vessels are consistently 20 pixels and the segmentation results have a consistent distance of only a single pixel to the boundary of the vessels, it is beyond any doubt that the segmentation is very accurate. However, the actual quantitative accuracy is only 90% (18/20), albeit there is only a single pixel difference for a large vessel with a consistent width of 20 pixels. Hence, it is reasonable to give a tolerance when assessing the agreement between the computer results and the manual delineation. Typically, a higher tolerance is needed for an image with a larger resolution, because the vessels with the same width may have more pixels.

When validating the performance of retinal vessel segmentation algorithms, most available approaches computed the performance measures, such as accuracy and sensitivity, by assessing the overlapping between manual delineations and computer results in area. Given the fact that small vessels typically have much smaller areas as compared with large vessels, area-based measures actually gave much higher weights to larger vessels. To overcome this limitation, we proposed to assess the segmentation performance by quantifying the agreement between manual delineations and computer results in centerlines. An established skeletonization algorithm was applied to the manual delineations as well as to our computer results.⁴⁴

We are aware that the multiscale strategy has been widely explored by available approaches from different perspectives. For example, the matched filtering method proposed by Hoover *et al.* enhances vessels with different widths by dynamically changing the angle and the width of the filter.²² Considering that the intensity of retinal vessels varies in different regions of an image, Hoover *et al.* and Akram and Khan used multiple thresholds to identify vessels.^{22,39} Al-Diri *et al.* used the tramline algorithm to first identify the centerline of retinal vessels and then applied a segment growing strategy to progressively identify retinal vessels.²⁸ After identifying an initial set of seeds using predefined rules, Vlachos and Dermatas performed a line track procedure to identify retinal vessels at multiple scales in terms of vessel diameter.¹² Wang *et al.* used a multiresolution Hermite model to segment retinal vessels.²¹ Sofka and Stewart incorporated several multiscale measures, including vessel confidence measures, matched-filter response, and vessel boundary measures, into a machine learning based classifier to identify vessels.⁴⁵ As compared with these approaches, our method innovatively quantified the contrast of a fundus image at multiple scales and then fused them in a progressive manner with consideration of both their spatial difference and continuity. At the same time, we noticed a limitation associated with the proposed algorithm: small vessels may be associated with relatively overestimated widths (Figs. 9 and 10). This issue may be caused by the multiscale characteristic of this method, which has somewhat smoothing effect as presented by Eq. (1), and the partial volume effect exhibited by small vessels. For small vessels, it is difficult to know their exact boundaries which could be affected by the existence of image

noise and partial volume effect. A potential solution is to apply a method similar to the well-known active model that allows the boundary of the vessels to evolve dynamically under predefined external and internal forces to the locations these forces reach a state of balance.⁴⁶

5. CONCLUSION

An algorithm was described in this study to automatically identify retinal vessels depicted in color fundus photographs. Three components are involved in implementation, including contrast quantification, image fusion, and central light reflex region filling. Experiments on three publicly available databases that contain both diseased and healthy subjects and both low and high resolution images validated its feasibility and performance.

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