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Early Detection of Diabetes Retinopathy by New Algorithms for Automatic Recognition of Vascular Changes

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Abstract: Diabetes mellitus often results in diabetic retinopathy caused by pathological changes of the retinal vessel tree. Early detection of these changes can delay the disease. Image processing can reduce the workload of screeners and can play a central role in quality assurance tasks. Therefore we aimed at the refinement and development of image processing algorithms to improve the quality and cost effectiveness of screening and diagnosis of diabetic retinopathy. In order to support ophthalmologists in their routine and to enable the quantitative assessment of vascular changes in colour fundus photographs a multi-resolution approach was developed which segments the vessel tree efficiently and precisely into digital images of the retina. The vessel tracker aims at determining as correctly as possible the retinal vascular network captured on a digital image irrespective of its origin. In addition to the tracker, algorithms were developed to detect the optic disk, bright lesions such as cotton wools spots, and dark lesions such as haemorrhages. The following classification of veins and arteries identifies arteries in 78.4 % and veins in 66.5% correctly. This helps selecting conspicuous images from a great number of patients.

Key words: Diabetic retinopathy, retinal vascular tree, vessel tracking, image processing

Introduction

Diabetic retinopathy (DR), which is a result of long-term diabetes mellitus, is one of the leading causes of blindness in the western countries. It causes pathological changes of the retinal vessel tree such as microaneurysms, intraretinal microvascular abnormalities, venous beading and neovascularisations as well as haemorrhages, exudates and retinal oedema. In order to prevent these complications it is important to treat the patients as early as possible.

At present routine vascular modifications are examined either by direct inspection (ophthalmoscopy) or by analysing photographic documentations of the ocular fundus (fundus photographs). In order to improve the assessment of the retina status image processing methods are needed to extract relevant quantitative data about changes of the retinal vessel tree. A vessel-tracking algorithm can extract data about the vessel course and contour [1, 2]. This data can be analysed by the ophthalmologist or used for automatic recognition of vascular changes like vasoconstrictions, vasodilatations, venous beading and new vessels. The extraction and analysis of retinal vessels has been performed in various ways [1, 5, 8, 9]. Any automatic method has to solve the problem of false segmentation, which arises from inhomogeneous illumination of the eye background. This produces colour changes within one image. Besides, there are no standards for quality of the image, such as contrast or brightness.

The work was performed as a part of the TOSCA project (Tele-Ophthalmological Services - Citizen-centred Applications), which was sponsored by the European Union.

Methods and Material

Material

Our vessel tracker was developed using 248 colour images: 64 with no diabetic retinopathy (DR), 64 with mild to moderate DR, 60 with severe non-proliferative DR and 60 with proliferative DR. The images had a resolution of 760x570 pixels, 24 bit – 16.8 millions colours in Tiff format.

Most of the images were captured by a Canon NM6 with a 45° acquisition angle. Some images were obtained with a Mydriatic Kowa ProII, 30°; some by both fundus cameras. From each of the groups ("No DR", "Mild-to-moderate DR", "Severe non proliferative DR" and "Proliferative DR") 15 cases were randomly selected. For each patient four retinal fields were examined: right eye temporal, right eye nasal, left eye temporal and left eye nasal. Factors such as sharpness, brightness or readability did not affect the selection. Some images with moderate or even severe cataract were included.

Automatic Vessel Tracking

For pre-processing all pixels darker than 17% of the maximum brightness in the image are removed. 17% was empirically found, and proved to be correct for all photographs analysed. After having selected the green channel which had proved to provide the best contrast in a colour fundus image the a priori maximum vessel width in the image is decided upon. Numerous tests

proved 1/60 of the image width in pixels to be the optimum.

The algorithm is started from a grid which consists of 40 horizontal and 40 vertical lines independent of the resolution, and overlies the image. Can [5] proved 40 lines to be the optimum. For each grid line the local minimum of the grey-value is determined. It has to be at least 5% darker than the local maxima to the left and to the right, and the local maxima to the left and to the right have to be less than the a priori determined vessel width apart (see Fig. 1A). An example for detected seed points can be found in Fig. 1B. The seed point candidates are evaluated by determining already detected vessel segments, and by the direction of the untracked vessel at the seed point.

In order to find the best direction for the vessel tracker, each of the following steps is performed in three different directions (see Fig. 2):

1. A rectangle window with twice the size of the vessel width is taken from the image and rotated in the direction that is to be analysed.
2. The rectangle window is smoothed along this direction and summed up to generate a one-dimensional vector. The length of the Gaussian filter used is adjusted to the vessel width.
3. The minimum and the maximum of the gradient of this vector are defined as the left respectively the right edge of the assumed vessel.
4. The location of these edges as well as their strength determines the result.

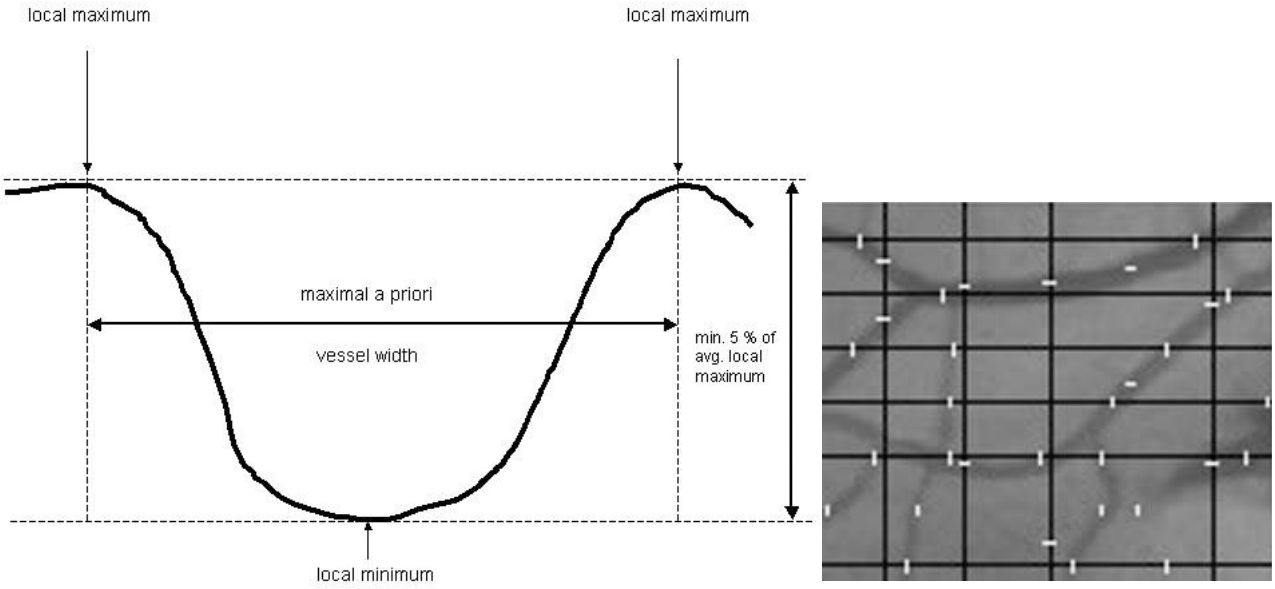

Fig. 1. Pre-processing. Search of a local minimum: A local minimum is accepted as a seed point, if it is at least 5% darker than the average local maxima, and not wider than the a priori determined vessel width (A). White spots show the location of detected local minima on the black grid lines (B).

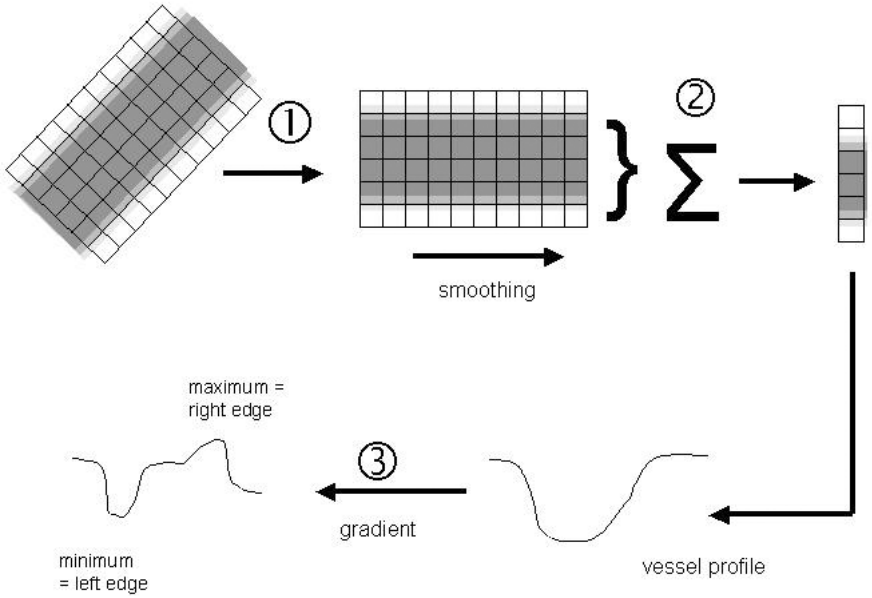

Fig. 2. Directional-Smoothing Subfunction. To analyse the strength of vessel edges in a given direction, the following tasks are performed:
1. A rectangle is taken out of the image and rotated into the direction to be analyzed
2. A directional Gaussian smoothing filter is applied, and the result summed up, to generate a one-dimensional vector.
3. The maximum and minimum of the gradient of this vector are at the right and the left edge of the vessel.
4. The value of the gradient is a measure for the strength of the edge.

The tracker has to automatically detect the centre line of the vessel and the progression of the vessel width along this centre line. Therefore, the tracker is given the position of the seed point, the direction of the vessel, and the width of the vessel, as calculated by the seed point evaluation. It performs the following tasks in a loop:

- The centre point is moved 1/8 of the vessel width along the vessel direction.
- Three windows in different directions (vessel direction, and 22.5° left and right to the vessel direction) are tested by the directional-smoothing sub-function for their strongest edge. The window which shows the strongest edges after smoothing determines the new direction of the vessel.
- The new vessel width is calculated starting from the position of the edges.
- Based on the new width and on the position of the edges, the centre point can be moved to the centre of the two edges, which is the centre of the vessel.
- The loop is terminated, when the vessel ends or when it hits another vessel that has been traced before. Indicators for an end of vessel are the new centre point being outside the image area, too low a contrast, vital changes of the new vessel width. In case the vessel has ended the vessel segment is not passed to the "Branch- and Crossing-Point Classification". If, however, the new centre point is on an already traced vessel segment, the vessel segment is passed to the "Branch- and Crossing-Point Classification".

The centreline, the progression of the width and the direction of each point of the centreline, as well as the branch- or crossing points, are stored for each vessel segment. This information can be used to plot the detected vessel segments into the image as shown in Figure 3.

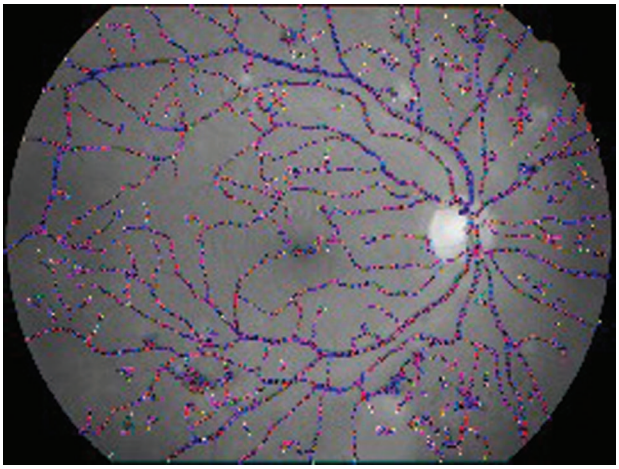

Fig. 3. Traced vessels with centreline (red) and width (blue).

Detection of Haemorrhages

Points which the vessel tracker has discarded as unsuitable for vessel tracking are used as starting points for the detection of haemorrhages. They are defined by an automatic region growing process (Fig. 4).

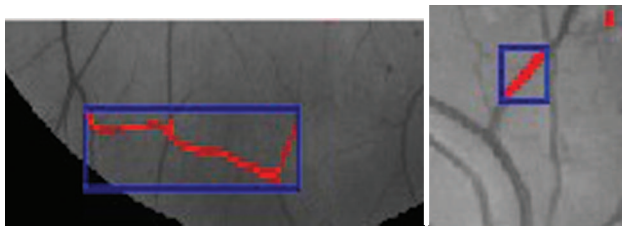

Fig. 4. Falsely detected vessels. The unlikely relation of length and width indicates a falsely identified vessel. In the case shown above the sides of the surrounding rectangle are almost equally long (A). In case the rectangle contains too few marked pixels it is likely that a vessel has been wrongly identified (B).

Detection of the Optic Disc and Bright Lesions

The optic disc was taken as the starting point for vessel classification.

In order to identify the optic disc a morphologic closing algorithm removes the dark vessels inside the optic disc and leaves only the bright optic dic. As the border between the retina image and the black surroundings would interfere, the border is removed with a template. Circle Hough transformations for different radii are performed. The strongest response provides centre and radius of the optic disc.

An algorithm was built to identify bright lesions which might interfere. Local minima are tracked along the grid lines and used as seed points for a region growing algorithm which uses the same modification and discarding criteria as the one described above for the haemorrhages. An example is presented in Figure 5.

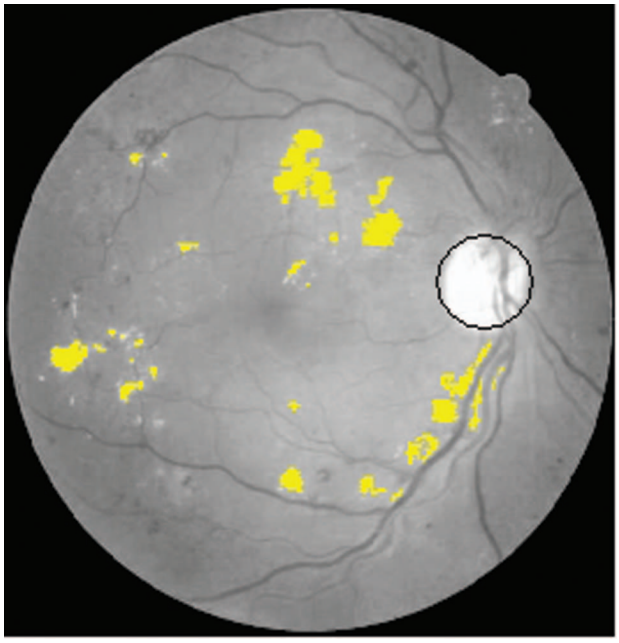

Fig. 5. Automatically detected bright lesions (yellow).

Classification of Arteries and Veins

The principle of the discriminant analysis is to separate two or more groups and to classify new cases. The present problem was to perform a discriminant analysis between two groups coded as "arteries" and "veins" comprising sample sets of 213 and 811 cases with feature vectors derived from images of the eye's fundus. The group identification for each case was assessed by visual evaluation. The features were composed of the following variables: Greyvalue, vessel width and reflection. Each case was classified in the group that yielded the highest posterior probability. At each step, group classifications based on a re-classification were evaluated and presented in a classification matrix. Furthermore, a jack-knifed-validation, i.e. a hold-one-out classification was performed to reduce the bias in the group classifications. This means that each case which is being classified according to the classification functions which is computed from all the feature vectors except that case being classified. From the total set of 213 arterial feature vectors 164 cases were classified correctly. Accordingly, from 325 venous vectors 216 cases were allocated in the vein group.

Results

The main goal of the vessel tracker was to identify the retinal vascular network as correctly as possible, regardless of the source (digital image or digitised by a scanner) of the tiff image. Even the resolution, which often proves to be a limiting factor did not interfere with the algorithm. These are major developments compared to many previous studies. The output is a monochromatic retinal image, on which vessel tracings are superimposed by red lines running along the centre of the vessels. Width and direction in each point are marked by blue segments, the length of which indicates the vessel diameter in that particular point.

The largest vessels were usually tracked correctly if their resolution was sufficient. The temporal vascular arcades could be traced in almost all the images. Due to its dimension and its contrast it was particularly easy to recognize the venous tree. Even if tracking could not be followed due to vessel fragmentation, its distal prolongation could be found. Vessels running too close to the border of the image were often ignored, because they could be centred only partially or insufficiently. The "local" vessel dimension, however, was always shown precisely. Light reflexes which are often observed in retinas of young patients did not interfere with the vessel tracker; nor were discrete lesions ever identified as vessel segments. Small veins were easier detected than small arteries. These required good quality images, preferably on a bright retina. The cameras also influenced the results: Kowa cameras gave better results than Canon's. Additional tests on high-resolution images obtained from other fundus cameras reached in some cases 100% of vessel mapping. However, vessels with many direction changes ("tortuous") remain difficult to trace.

The detection of venous beading proved to be unsatisfactory for several reasons:

- an exact definition of venous beading is still missing;
- the database for marked images with venous beading did not provide a basis for implementing a working algorithm;
- an algorithm was hard to determine, because the venous beading occurs mainly in the small distal veins;

With the help of the discriminant analysis, which selected between two groups coded as "arteries" and "veins", 164 cases from the total set of 213 arterial feature vectors could be classified correctly. Accordingly, from 325 venous vectors 216 cases were allocated in the vein group. The quantitative results are presented in Table 1.

Discussion

There have been many approaches to vessel detection in retinal images in the past (Akita [1, 2, 3], Tanaka [19], Chaudhuri [6] and Hoover [13]. While Gardner [11], Sinthanayothin [16], or Goldbaum [12] investigated different combinations of edge detection or matched filter methods with artificial neural networks, others used various kinds of edge maps for vessel tracking. Wu [22] and Meehan [16] analysed the vessel width and used edge detectors for finding a suitable piece of vessel. Gagnon [8] utilized a recursive dual edge tracking based on Canny algorithm and connectivity recovering starting at the optic disk. Lalonde et al. [9] also improved the handling of bifurcations and broken or missing edges by adding additional features e.g. seed points for further tracking to a non recursive paired tracking for vessel extraction. Kochner [14] showed the use of steerable filters. Tamura [18] traces the vessels with a second order derivative of Gaussian function detects after having detected the optic disc with a Hough transformation technique. Gao [10] only measures the vessel diameter. The exploratory tracing algorithm developed by Can [6] and Shen [17] provides useful partial results. It scales well with image size and requires only a small number of parameter

Table 1. Results of the stepwise discriminant classification (in brackets the results of the jack-knifed classification)

Group	Percent correct	Number of cases classified into group	
		Artery	Vein
Artery	78.4 (77.0)	167 (164)	46 (49)
Vein	66.5 (66.2)	109 (110)	216 (215)
TOTAL	71.2 (70.4)	276 (274)	262 (264)

settings. Wink [20] presents a method that uses a vectorial multiscale feature image for wave front propagation between two or more user defined points to retrieve the central axis of tubular objects (vessels) in digital images. Barber [4] describes a method to analyse 3D data sets by allowing the manual and semi-automated tracking and delineation of the vascular tree, including the measurement of vessel diameter.

The main problems in former studies had been the need for user-interaction, the presence of the optic disk or intensive computations due to pre-processing. Other difficulties were posed by the use of large kernels or by processing each single pixel in the image, poor scaling with the image size or not providing partial results if there was a computational deadline. Poor handling of bifurcations and of broken or missing edges often caused an unsatisfying result of vessel tracking. Additionally, many algorithms need a particular environment and definite image resolution or image size.

The newly developed algorithm for the Multi-Resolution Retinal Vessel Tracker overcomes many problems described by Coatrieux [7]. The handling of the discontinuous regions by relying on local contrast, edge information and noise is much improved. The computational efficiency of the newly developed algorithm makes it attractive especially in case of high-resolution images (2K x 3K).

Conclusion

Diabetes is a disease which can lead to blindness. This can be prevented by early treatment based on screening examinations. The developed algorithm and the classifier provide very good tools for screening procedures. These can be used to identify pathological changes in the retina to be followed by a more detailed screening by an ophthalmologist. The newly developed algorithm for the Multi-Resolution Retinal Vessel Tracker shows robust and accurate handling of branching and crossover points. Its computational efficiency makes it attractive especially in case of high-resolution images.

The work was part of the TOSCA project (Tele-Ophthalmological Services - Citizen-centred Applications), which was sponsored by the European Union. The main impact was on the evaluation of existing algorithms for vascular changes and on overcoming existing deficiencies. Thus the described algorithms were developed. The first validation showed promising results. A detailed evaluation study is being performed at the moment. The results will be integrated. We expect the system to be used in routine in the near future.

Pathological changes of the retinal vessel tree often caused by long-term diabetes mellitus need to be identified and treated at the earliest possible point of time in order to prevent complications. At present routine vascular modifications are examined either by direct inspection (ophthalmoscopy) or by analysing photographic documentations of the ocular fundus (fundus photographs). In order to improve the assessment of the retina status image processing methods are needed to extract relevant quantitative data about changes of the retinal vessel tree. A vessel-tracking algorithm can extract the vessel course and contour. General practitioners without any special ophthalmologic knowledge could produce images from patients' retinas and send them for classification. Thus more patients could easily be screened in a very efficient way.

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