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Computerized Analysis of Narrow-field ROP Images for the Assessment of Vessel Caliber and Tortuosity

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Abstract—**Retinopathy of prematurity (ROP) is a disease involving abnormal development of retinal vasculature in premature infants, which might eventually lead to retinal detachment and visual loss. The quantitative assessment of vessel morphological features, such as width and tortuosity, can improve the clinical diagnosis and evaluation of ROP. We propose here a computerized system for the vascular analysis of narrow-field premature infant images. It is based on the manual drafting of the vessel axis, followed by automatic Canny filter edge extraction and automatic caliber and tortuosity estimation. We implemented this method as a web-based tool, ROPnet, which allows the quantitative assessment of vessel width and tortuosity simply using a web browser. To test the accuracy of the estimated parameters, fifteen narrow-field (30°) retinal images were acquired in infants with a non-contact fundus camera and analyzed with ROPnet. We compared the results with the corresponding ground-truth values derived from manual analysis. Average widths and tortuosities estimated with ROPnet vs. manual ones showed a correlation coefficient of 0.96 and 0.90, respectively.**

I. Introduction

Many retinal diseases are characterized by changes in retinal vessels. A common condition associated with retinopathy of prematurity (ROP), a disease involving abnormal development of retinal vasculature in premature infants that might eventually lead to retinal detachment and visual loss, is just the increase of vascular dilation and tortuosity, as initially reported by Owens [1]. Later on, Wallace et al [2] and Freedman et al [3] showed that vessel diameter and tortuosity could be used to indicate the risk that ROP would progress to a stage requiring treatment.

As pointed out in [4]-[6], in order to reduce the risk for premature infants and decide if a prompt therapy is necessary, regular checkups are needed during the first months after birth. Therefore, any solution that can help ophthalmologists to easily identify and objectively quantify signs of ROP before it has progressed to the point where sight may be seriously compromised may be of great clinical benefit.

To this end, the use of a portable, non-contact narrow-field fundus camera, such as the NM200D (Nidek Co., Gamagori, Japan), can provide important advantages for intensive screening, such as ease of use, portability, non-invasive acquisition and low cost. With the same purpose, many systems for computer aided diagnosis have been recently developed to increase the quality and productivity of ophthalmologists' screening. Their aim is to allow to accurately measure and quantify retinal vascular geometrical and morphological properties in premature infant images [7]-[10]. Despite their potentially interesting results, all of these programs have some drawback or limitation and none is accessible through the web nor is widely used outside the developing institutions. Moreover, almost all of these programs have been aimed at wide-field digital images, such as those acquired with the RetCam imaging system (Clarity Medical Systems Inc., Pleasanton, CA, USA), and only one was tested with narrow-field fundus images [11].

We propose here a new computerized method for the vascular analysis of narrow-field infant images. These images usually exhibit blur and low contrast, because of the lack of clarity of the eye media and the technical difficulties in image acquisition. These aspects represent a serious obstacle to the automatic identification of vascular structures. To cope with this problem, the proposed method requires the user to manually select the vessel to be analyzed by drafting its centerline. From this manual information, vessel borders are then extracted using an automatic procedure and vessel calibers and tortuosity are computed.

The method we propose was implemented in a system called ROPnet, which was developed considering two main user-related purposes: the accessibility, at any time, by users from all over the world, and the user-friendliness of the system. The first goal was achieved by making the tool available through a web browser over an internet connection, the latter by developing a graphical user interface (GUI) to allow the client to intuitively interact with the server-based application that performs the analysis on retinal images.

II. Methods

The vessel to be analyzed is at first selected by manually drafting the vessel centerline. After image enhancement, all vessel edge points are extracted by means of a Canny filter. Refined axis and diameters along the vessel are then identified by appropriately associating pairs of points on opposite edges. From these results, vessel width and a tortuosity index are computed.

The vessel tracing methods and the functionality of ROPnet are described in detail in the following sections.

A. Image preprocessing

At first, the green channel is extracted from the original RGB retinal image, since it provides the best quality and highest contrast for vessel structures over the background.

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The vessel to be analyzed is manually chosen by the user, quickly drawing a curve that approximates the position of its centerline. A region of interest (ROI) is automatically extracted around the selected vessel, in order to limit the processing area and thus reduce the computational time. The ROI is then filtered with a two dimensional bilateral filter [12], which is a combination of domain and range filtering techniques for edge preserving and smoothing. This solution reduces the noise and the gray level artifacts inside the analyzed vessel and in the background, making the subsequent vessel border extraction method more robust.

B. Vessel border extraction

A set C of candidate edge points is provided by an edge detector algorithm based on the Canny technique [13]. C usually includes points belonging to the edges of the selected vessel, but also to the edges of other vessels possibly present in the ROI, or to noise or artifact regions.

We need to discard these spurious edges and to identify two subsets of points, $EPR \subset C$ and $EPL \subset C$, that lay on either of the two actual edges of the selected vessel. To this aim, C is split into two subsets, L and R, including points that lay on the two opposite sides with respect to the user-drawn vessel centerline a. The distance between the barycenter of L and R provides ρ_E, an initial rough estimate of the average width of the vessel.

The vessel centerline a is divided into M parts along its length and every sub-segment of a can be expressed in curvilinear coordinates as a curve $a_p(i)$, with $i \in [1, \dots N_p]$ and $p \in [1, \dots M]$. Moving stepwise and simultaneously along all the sub-segments a_p, at the i-th step we consider a segment d_p^i orthogonal to the direction of a_p and centered in $a_p(i)$. The length of every segment d_p^i is set to the estimated average vessel width, (which at the beginning of the procedure corresponds to ρ_E) and the pair of points $epl_p^i \in L$ and $epr_p^i \in R$ having the minimum distance from the extremes of d_p^i is chosen among all the points in L and R, respectively. During iterations, the estimated vessel diameters (i.e., the distances between the *epr* and *epl* identified so far) are used to obtain a more accurate evaluation of the average width of the analyzed vessel: after the generic i-th step, a new pair of *epr* and *epl* is selected in each of the M regions and the average vessel width ρ_{AVG} is updated by averaging the distance between the $i*M$ pairs of edge points *epl* and *epr* identified so far.

As described above, M different parts of the vessel (i.e., the M sub-segments a_p) are simultaneously analyzed: in this way, ρ_{AVG} is iteratively updated by taking into account vessel diameters located in different regions of the vessel and so the estimated average vessel width is less affected by local imprecisions in diameter, due to possible noisy or blurred areas. An example of the simultaneous analysis of a vessel, in three different regions, at progressive iterations, is presented in Fig. 1.

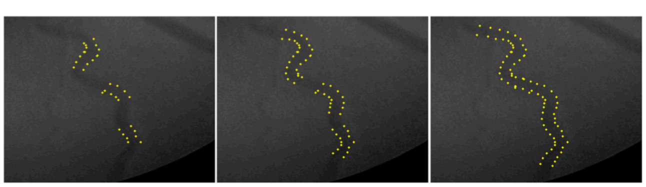

Fig. 1. An example of the simultaneous analysis of a vessel in three different regions at progressive iterations.

C. Correction of unreliable diameters and border regularization

In some critical areas along the vessel (e.g., low contrast areas, or areas where two vessels cross), edges might not be visible and the selected pairs of points *epl* and *epr* might not be placed over the true vessel edges. The average width ρ_{AVG} is used as a threshold in the criterion to accept or reject edge points. If

$$\frac{|d(epl,epr)-\rho_{AVG}|}{\rho_{AVG}} < t \quad (1)$$

the points are accepted, otherwise two points *epl* and *epr* are created so that their distance is just equal to ρ_{AVG}. The threshold parameter t was empirically set to 0.25.

For the selected vessel segment, the steps described above provide two sets of points $EPR = \{epr_i,\ i = 1{:}N_{epr}\}$ and $EPL = \{epl_i,\ i = 1{:}N_{epl}\}$ sampling the two edges of the vessel. In some vessel sections, samples might be noisy or sparse, leading to an irregular border description. Regularity of vessel borders was achieved by means of interpolation. Being vessels continuous structures at least with their first derivative led us to use a cubic smoothing spline interpolation, which yields two curves *CR* and *CL*, laying on either vessel edge. The initial, manually drawn vessel centerline a is then updated with the curve VC, computed by taking the midline between *CR* and *CL*.

Local vessel widths along the axis are evaluated by measuring the distance between the curves *CR(l)* and *CL(l)* at each curvilinear coordinate l. A tortuosity index is evaluated for the selected vessel using an algorithm recently proposed by our group [14]. This algorithm proved to be very resilient to a sparse and noisy description of a vessel, which makes it perfectly suited for this application to ROP narrow-field infant images.

D. Web-based ROPnet system

The vessel tracking technique just described was implemented in a web-based system, named ROPnet, accessible via a web browser. To start the analysis, the user is required to connect to the ROPnet web site and login. For every user, a specific PHP session is created, together with dedicated memory allocation on the server. This allows to safely manage multiple simultaneous accesses.

Once logged in, the user can browse the local drives and choose the retinal image to be analyzed. The selected image is sent to the server, where it is temporarily stored until the analysis is finished. A pre-processing algorithm (described in Section II-A), aimed at enhancing the image contrast, is

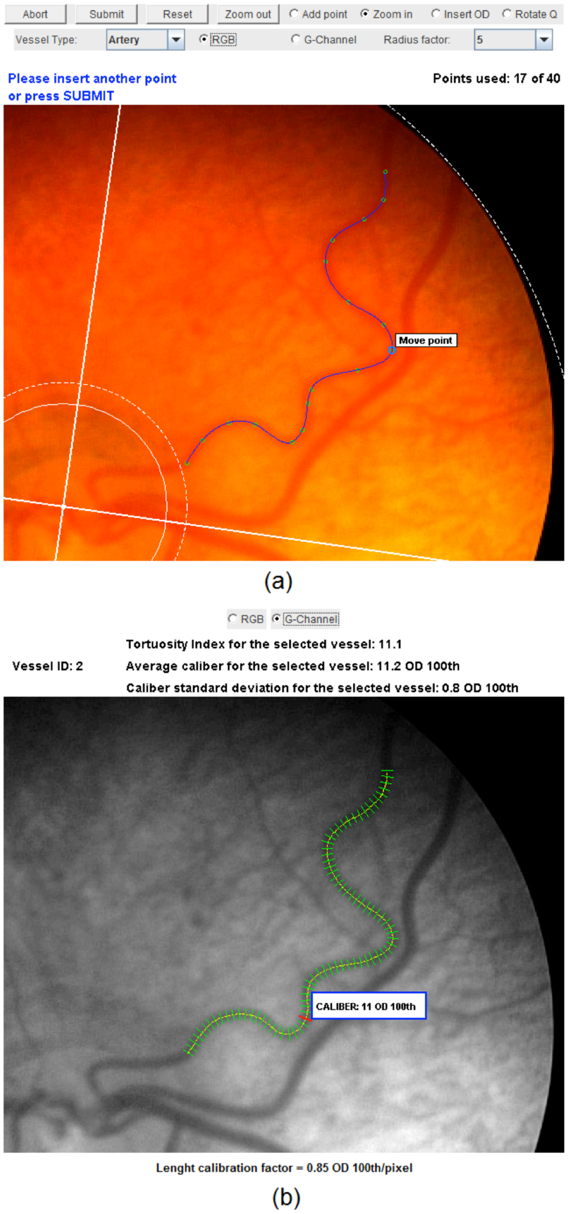

Fig. 2. The graphical user interface of ROPnet: the applet for the analysis setup (a); and results displayed (b).

then run server-side as a background process.

While pre-processing is running, the client is redirected to a web page including a Java applet (Fig. 2a), which displays the graphical user interface that allows the user to choose the vessel to be analyzed and to set the parameters needed for the analysis (i.e., to set up the image visualization, to define the optic disc position and the retinal quadrant subdivision, etc.). The applet sends the information acquired to the server, where vessel tracking and computation of clinical parameters are performed (see Sections II-B,C). When the analysis is completed, the server displays the results on a web page (Fig. 2b). The returned clinical parameters are the vessel tortuosity index and average width.

The user can then choose to analyze a new vessel on the same image, upload a new image, or log out from the ROPnet web site.

III. Materials

Fifteen retinal images were acquired with the non-contact camera NM200D (Nidek Co., Gamagori, Japan) in the Neonatal Intensive Care Unit at the Scheie Eye Institute, University of Pennsylvania or at the Division of Ophthalmology, Children’s Hospital of Philadelphia (both in Philadelphia, PA, USA). Images were acquired with a 30° field of view and saved in digital format as 1280x960 pixels JPEG compressed images. The average gestational age of the infants and average birth weight were 26 weeks and 816 grams, respectively. Average post menstrual age (PMA) at the time of fundus photography was 33 weeks.

To test the accuracy of measured vessel width and tortuosity, we used two different datasets of vessels, extracted from the 15 acquired images: for width Dataset A, including 12 vessels from five different images, and for tortuosity Dataset B, including 12 vessels from ten different images.

The vessels in Dataset A were chosen in order to cover the widest possible range of vessel widths. Ground truth reference width values were obtained with a manual segmentation of the vessel segments. Using a public-domain image manipulation program (GIMP v. 2.6.6, http://www.gimp.org/) a retina imaging expert identified on screen-displayed enlarged versions of the images all the pixels belonging to vessels. The same algorithm used in ROPnet was then used to estimate the width of the manually segmented vessels, which was then used as ground-truth reference.

The vessels in Dataset B were chosen so as to cover the widest possible range of tortuosities. The ground-truth reference for tortuosity consists in a manual ranking provided by an expert ophthalmologist who ordered the twenty vessels by increasing tortuosity.

IV. Results

The width of the vessels of Dataset A was measured with ROPnet and compared to the manual reference measurements. For both measurements, in every vessel segment a set of equally spaced diameters along the axis was measured and then averaged, in order to get the average vessel width. In Fig. 3a the scatter-plot of the manual vs. computerized average width in the 12 vessels is shown. A Pearson correlation coefficient of 0.96 was obtained.

As regards the vessel tortuosity estimation, we considered the correlation among manual and computerized rankings for the 12 vessels of Dataset B. In Fig. 3b the scatter-plot of the manual vs. computerized tortuosity ranking is shown. A Spearman correlation coefficient of 0.90 was obtained.

The analysis of a vessel with ROPnet takes on average less than one minute.

V. Discussion and Conclusion

A new semi-automatic system is proposed to identify the vessel structures in retinal infant images acquired with a narrow-field fundus camera. The technique for vessel tracking

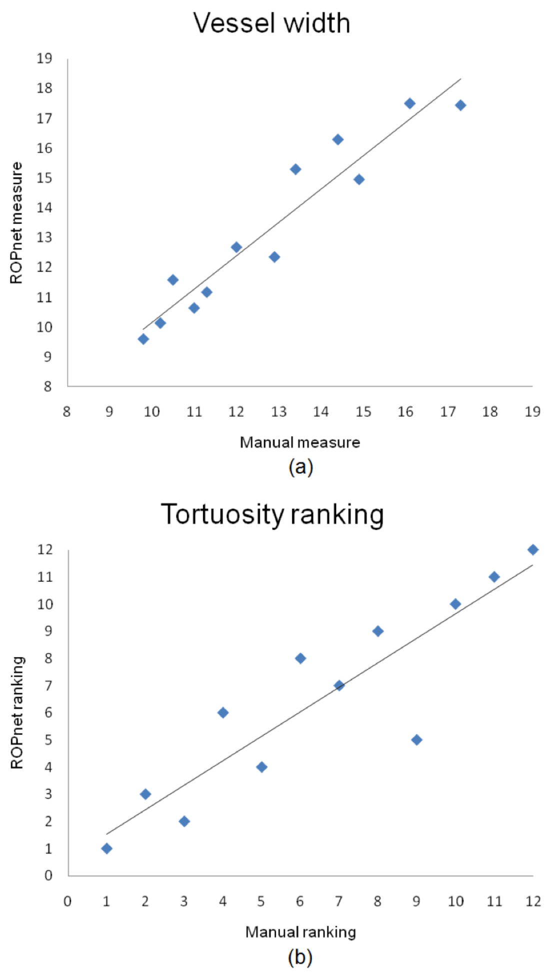

Fig. 3. Scatterplot of average width values: computer-aided evaluation vs. manual reference (a). Scatterplot of the tortuosity rankings: computer-aided evaluation vs. manual reference (b).

was specifically developed in order to overcome the difficulties related to the analysis of narrow-field images acquired in infants. The web-based tool proposed for vessel analysis allows extracting important clinical parameters, such as vessel tortuosity and width, with remarkable accuracy.

In the current version, the system allows the analysis of one vessel at any one time and we focused our attention on the reliability of estimated indexes. Future work will investigate if the indexes derived from several vessels in the same image can be properly combined to estimate clinical parameters at whole image / patient level. In this way, objective and reproducible quantitative information from computerized image analysis may provide a more reliable assessment of ROP in eyes at risk, reducing the variability of diagnosis related to poor inter-expert agreement [11].

The web-based solution and the user friendliness of the interface make the tool available to a wide range of users. Its adoption can improve the productivity of ophthalmologists' screening, being the diagnosis of ROP possible even far from the neonatal intensive care unit, where image acquisition could be referred to trained paramedical personnel. Moreover, the choice to run vessel analysis as a client-server application allows us to easily provide users with the latest version of the various algorithms.

A beta version of the ROPnet system is hosted at the website http://bioimlab.dei.unipd.it; it is already publicly available upon request to interested users.

Finally, as wide-field retinal imaging systems, such as the RetCam device by Clarity Medical Systems, are widely used in hospital settings worldwide for ROP evaluation in premature infants, a different version of ROPnet is being developed for wide-field retinal images acquired with the RetCam fundus camera.

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