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Quantification of Retinopathy of Prematurity via Vessel Segmentation

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Abstract. Retinopathy of prematurity is a disease that affects the eyes of many babies who are prematurely born. If the retinopathy is not detected in the days following birth, blindness may occur. Studies have demonstrated that by observing the blood vessels within the retina, the disease can be quantified at an early stage, and early treatment can save the baby's eyes. We have developed a new tool to assess retinopathy of prematurity. Our technique captures the image of the retina to extract and quantify both tortuosity and dilation of blood vessels. Our approach demonstrates a 80% sensitivity and 92% specificity in the prediction of retinopathy compared to experts, shows significantly reduced diagnosis time, and features clinical integration via speech recognition and glare detection.

1 Introduction

Retinopathy of prematurity (ROP) is an eye disease that occurs in some prematurly born babies. The last 12 weeks of a full-term delivery, from 28-40 weeks gestation, are particularly active for the growth of the fetal eye. The blood supply to the retina starts at the optic nerve at 16 weeks of gestation, and the vessels gradually grow out over the surface of the retina. The vessels reach the anterior edge of the retina and stop their progression at about the time of birth. Therefore, prematurely born baby's retinal vessels may be incompletely formed and drain poorly, leading to blindness.
Wallace et al. [9] [4] have shown that ROP can be accuratly and quickly detected by looking at the vessels within the retina. In particular, they demonstrate that tortuosity and dilation of retinal vessels are good predictors for ROP. Their system uses a lens to magnify a baby's dilated pupil and a video capture system. After the procedure, physicians compare the video images with 5 reference images, Fig.1, which are graded 0 to 4. Due to subjectivity of the comparison, this method can take as long as one hour per baby and, for some cases, there is a high inter-physician disagreement.

We have developed a new tool for evaluating retinopathy of prematurity. Our system includes a computer-aided diagnosis software which assess dilation and tortuosity automatically. We have also used digital video recording and speech recognition to facilitate the integration into the clinic. Our system is described next.

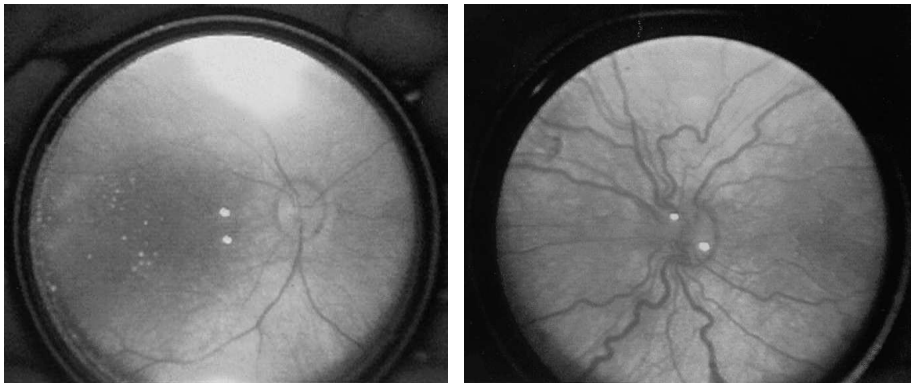

Fig. 1. Reference images for evaluation of retinopathy of prematurity. Grade 0(left) represents normal vessels and Grade 4(right) shows ROP

2 Methods

2.1 Overview of the system

Our system is composed of four parts: ens, digital video acquisition system, speech recognition library and image processing software. The lens is used to magnify the view through the baby's dilated pupil in order to improve blood vessel visibility. Radial distortions are minimal and, at most, minimally bias the image; the same lens is used to acquire the reference images. The digital acquisition system is composed of a head-mounted camera, Fig.2-left, which records the image the physician sees. The camera is composed of a lamp and two mirrors that coincide to form a monocular digital view. During the procedure the camera is connected to a laptop computer which can digitize still images from the video signal. The light beam from the camera and the lens can combine to introduce glare, and without precautions, the digitized image may be useless, Fig.2-right. Therefore, a real-time glare detector has been implemented; it produces a beep when too much glare is present in the live video.

Another important feature of our system is the addition of a speech recognition engine [7] [8]. In the clinic, the physician is often alone when capturing the images. Wearing a microphone clipped to their jacket, the physician need only

Fig. 2. The OMEGA 100 Head-worn indirect Ophthalmoscope from Heine Optotechnik(left). The light beam from the head-mounted camera reflects on the lens and produce glare(right)

to say "capture" to digitize an image. At the same time, the glare detector gives feedbacks on the quality of the image.Once the image is captured, the retinopathy grade estimation is computed in less than 30 seconds, much less than the time required to go from one baby to the next in the pediatric intensive care unit.
The estimation of the disease is done using a vessel segmentation method. This is described in the next section.

2.2 Vessel quantification

Retinopathy of Prematurity diagnosis is based upon visual inspection of retinal blood vessels. Martinez-Perez et al. [6] have developed a region growing technique combined with scale-space analysis to extract blood vessels in the retina. Leandro et al. [5] use a continuous wavelet transform combined with morphological operators to segment blood vessels within the retina. This last method does not use any model information and the output of the algorithm is a binary image representing the segmentation. On the other hand, our method uses geometric information by considering blood vessels as tubes and better supports more complex measures on the extracted data such as tortuosity and dilation. Based on the extracted vessels, the four quadrants of the retina are identified and then a grade is determined via classification using a trained neural network. The vessel extraction is based on the work of Aylward et al. [1] which extracts blood vessels from 3-dimensional images using a scale space technique with subvoxel accuracy. Our algorithm traverses the ridge, $\boldsymbol{F}$, using the Hessian at point x. We define α and β as ascending-ordered eigenvalues of the Hessian at x and, $\boldsymbol{u}$ and $\boldsymbol{v}$ as the corresponding eigenvectors of the Hessian. We then define the directional derivatives: $\boldsymbol{P} = \boldsymbol{u} \cdot \boldsymbol{F}$ and $\boldsymbol{Q} = \boldsymbol{v} \cdot \boldsymbol{F}$. Therefore, if x is exactly in the middle of the ridge the following conditions must hold: $\alpha < 0$ and $\boldsymbol{P} = 0$.

Given an initial starting point close to the ridge, the intensity ridge is computed to minimize $\boldsymbol{P}$ using a direction search with respect to the Hessian. The line search is performed from x in the direction of $\boldsymbol{u}$ to find the local minimum of $\boldsymbol{P}$. If the resulting minimum is not within the tolerance a new initial point is required.
The initial starting points are defined by looking at minimum intensity values along a circle centered on the optic nerve. We assume that the optic nerve is located close to the center of the lens, this is a clinical requirement. Thus, a 2-dimensional Hough transform is used to detect the lens and from that the approximate center is calculated. Note that the initial starting point can be anywhere along the ridge, i.e. it does not have to located at one of the ends of the vessel.
When the ridge is found, a ridge traversal technique is used to extract the vessel. From the point x_i on the ridge, the approximate tangent direction $\boldsymbol{t_i}$ is defined as $\boldsymbol{v}$ the maximum egeinvalued eigenvector of the Hessian computer at x_i. The direction of the ridge traversal is maintained by multiplying $\boldsymbol{v}$ by the sign of the dot-product of $\boldsymbol{v}$ and the previous tangent direction $\boldsymbol{t}_{i-1}$.

$$\boldsymbol{t_i} = \text{sign}(\boldsymbol{v} \cdot \boldsymbol{t}_{i-1})\boldsymbol{v} \tag{1}$$

The approximate normal direction at x_i is given by $\boldsymbol{u}$ and specify a line that the local ridge passes through. Considering smoothness, if that line is moved by a small amount in the tangent direction, the ridge should continue to pass through that line. Therefore, the ridge will exist as a local maximum on that shifted line, and the ridge criteria is tested along that line and if criteria are met, the maximum becomes the next ridge point x_{i+1} until failure.

The estimation of the radius at each point x is done by finding a local maximum of a medialness function.

$$\sigma_i = \text{argmax}_\rho(M(x_i, \boldsymbol{t_i}, \rho)) \tag{2}$$

The medialness function $M(.)$ uses an adaptive convolution kernel formed by a ring of boundary operator centered about x, align with the normal vector at x, and at a distance ρ from x. Therefore, an estimation of the radius at each point x along the centerline of the vessel is known and defines, after average, the dilation factor for the specified vessel. Tortuosity τ is defined as straight distance between the two end points (x_0,x_1) of the considered vessel over the geodesic distance l of the segmented model.

$$\tau = \frac{\|x_1 - x_0\|}{l} \tag{3}$$

After tortuosity and dilation estimations, quadrants are defined using the distance between vessels to form four clusters. The optic nerve is taken as the center of the quadrants, and initially quadrants have the same size. Then, the size of each quadrant is optimized to maximize the number of points from each tubes within the given quadrant so that tubes are not split between two quadrants.

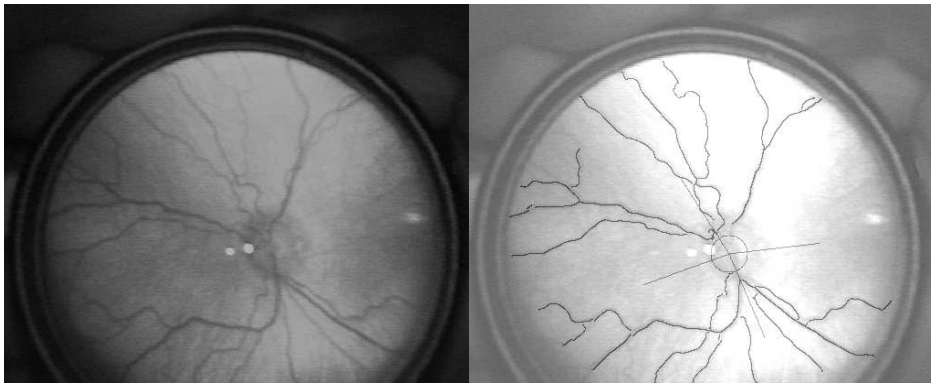

Fig. 3. Image captured from our acquisition system(left) and the resulting segmentation of blood vessels(right)

3 Results

Our algorithm has been tested on 20 premature infants, 10 normals and 10 representing various degrees of dilation and tortuosity. These 20 posterior pole images were analyzed by both our algorithm and two independant blended examiners experienced in the diagnosis of ROP. The standard photograph, Fig.4, obtained from the CRYO-ROP study [2] representing the minimum degree of dilation and tortuosity required for plus disease was also digitized, analyzed, and used as a numeric threshold for the automated determination of plus disease.

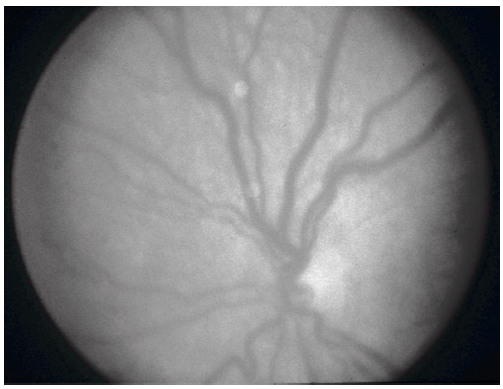

Fig. 4. Standard photograph obtained from the CRYO-ROP study

The examiners agreed on the presence or absence of plus disease in 17 of 20 cases. Of the five images determined to have plus disease by both exminers, four were calculated to have plus disease by our algorithm (80% sensitivity). Of the

12 images without plus disease, 11 were computed to not have plus disease (92% specificity). The examiners disagreed on the presence of plus disease on three images, and all three were calculated by our method to have dilation and tortuosity which was greater than normal but insufficient for plus disease. Fig.5 and Fig.6 report the results obtained. The quantification of plus disease is determined positive if at least two of the four quadrants have higher tortuosity and dilation than the reference image. It is important to consider both dilation and toruosity in the estimation process. The reference image has been normalied to have an average tortuosity and dilation of 10. The test images are then normalized with respect to the reference image.

	Normal	Pre-plus disease	Plus disease
Number of images	11	3	5
Number determined by computer to have plus disease	1	0	4
Number with >2 quadrants with >10 tortuosity units	2	1	4
Number with >2 quadrants with >10 dilation units	5	1	5
Average tortuosity (tortuosity units)	6.5	11.3	15.5 (p=0.001)
Average dilation (dilation units)	10.3	10.4	11.2 (p=0.12)
Average number of quadrants with >10 tortuosity units	0.6	1.7	3.0
Average number of quandrants with >10 dilation units	1.5	1.7	2.8

Fig. 5. Results obtained on 20 children prematurely born

		Examiners		
		Plus disease	Not plus disease	Total
	Plus disease	4	1	5
Computer	Not plus disease	1	10	11
	Total	5	11	16

Fig. 6. Examiner vs. Computer quantification. Our algorithm shows 80% sensitivity and 92% specificity

4 Discussion and Conclusions

Our Retinopathy of Prematurity detection system shows the same accuracy as experts and the entire procedure runs in less than 3 minutes. Integration into the clinic, using speech recognition and glare detection, has made this system useful to physicians. Overall assesment time has been decreased by 70%. Our software was implemented using the Insight Toolkit [3]. Aspects of this work have been licensed (patent pending) to Medtronic Inc. (Minn., MN) and R2 Technologies (Los Altos, CA).

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