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Comparison of Reliability of the Eye Optic Disc Cup and Pallor Areas in Glaucoma Diagnostics

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A B S T R A C T

The aim of this paper is to compare the glaucoma diagnostic reliability of two optic disc parameters: the relative cup area size determined by the Heidelberg retina tomography and the relative pallor area size determined by the proposed algorithm of the optic disc image analysis. Both parameters were measured for 240 normal healthy eyes and 240 glaucomatous eyes. The diagnostic reliability of studied parameters were compared using normalized distance d of their statistical distributions obtained for normal healthy and glaucomatous eyes and by comparison of area sizes under their ROC (Receiver Operating Characteristic) curves. The normalized distances were 2.19 or 1.73 and the area sizes under ROC curves were 0.95 or 0.89 for relative cup or pallor area size. Both considered relative parameters are significantly influenced by the glaucoma and can be used in its diagnostics. The designed pallor analysis is less diagnostic reliable than the analysis of the cup.

***Key words**: Cup, pallor, glaucoma, laser scanning tomography, image analysis*

Introduction

Early detection of glaucoma is necessary for effective treatment of this disease. One of effective methods of glaucoma detection is the determination and analysis of the color and shape of the optic nerve head (i.e. optic disc, OD). Especially, the typical symptoms of glaucoma are the enlargement of the optic disc cup and the rise of the pallor area of the cup[1,2]. The cup area can be exactly detected and subsequently numerically represented by the laser scanning tomography method[3–5]. For the pallor detection, a suitable computer algorithm of digital color photography analysis of the optic disc can be used. We designed and verified the new image analysis method of pallor detection and its numerical representation. For diagnostic evaluation of the proposed relevant pallor numerical parameters, the suitable automatic evaluation algorithms were designed and discussed[6]. In this paper, the diagnostic reliability of the above-mentioned numerical parameters of the pallor were compared with the diagnostic reliability of the common parameters obtained by the laser scanning tomography.

Subjects and Methods

Subjects

The chosen numbers of 240 eyes of 120 normal healthy subjects and 240 eyes of 120 subjects with the open-angle glaucoma were considered in our investigation. The examined normal healthy subjects had the age range from 14 to 76 years with the average of 46 years and with the standard deviation of 13 years. The glaucomatous subjects under examination had the age range from 10 to 82 years with the average of 51 years and with the standard deviation of 16 years. The reported medical diagnoses were carried out on the basis of the subjective evaluation of independent measurement of the intraocular tension, visual field, enlargement of the cup using the laser scanning tomography and of subjective observation of the thickness of the retina nerve fibre layer. All diagnostic examinations were performed by the same ophthalmologist.

Method for the cup analysis

The cup area was represented by the relative quantity C/D, which means the ratio of the representative cup area and the representative area of the total optic disc. The required representative areas were determined by the common laser scanning tomography method, especially using Heidelberg retina tomograph[4,5].

The used laser tomographic scanner (LTS) is based on a sequential point-by-point imaging and a confocal laser scanning microscopy. In the LTS device, a suitable diode

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laser source of the dominant wavelength 670 nm was focused by the optical system of the LTS and of the eye to the focal point situated on the optic disc. The laser beam scans point-by-point the optic disc by moving the focal point in the perpendicular direction to the optical axis of the scanning device at the constant position of the focal plane. The scanned area was divided into 384x384 scanning points. The angular size of the scanned area was 15°. The light reflected from each single scanned point was separated from the incident beam and deflected to a detector, where it was registered and thereafter digitized and stored by a computer as a two-dimensional section image. During one investigation, the images were scanned up to 64 sections at different axial locations z of the focal plane. The axial location z is the location in the direction of the optical axis of the scanning device and it was measured according to a suitably selected reference plane. The typical distance between two successive axial locations of the focal plane was 62 mm. In the used confocal optical system shown in Figure 1, two pinholes are located differently: behind the laser source and in front of the detector, both optically conjugated to the focal point of the laser source. By this arrangement, the light reflected by the optic disc point placed outside the focal plane is not focused to the detector. Its detected optical intensity is markedly smaller than the detected optical intensity of the light reflected from the focal plane. Thus, an axial position z of each scanned point can be determined in virtue of analysis of the experimental dependence of the detected optical intensity of the section images on the focal plane position. Its maximum corresponds to the searched axial position z of the considered scanned point. Finally, the required three-dimensional map, which describes the dependence of z on the point position (x, y) in the above-mentioned reference plane, was constructed.

The plane representative margin of the optic disc in the reference plane was commonly approximated by a suitable smooth plane curve. Such a curve was found by

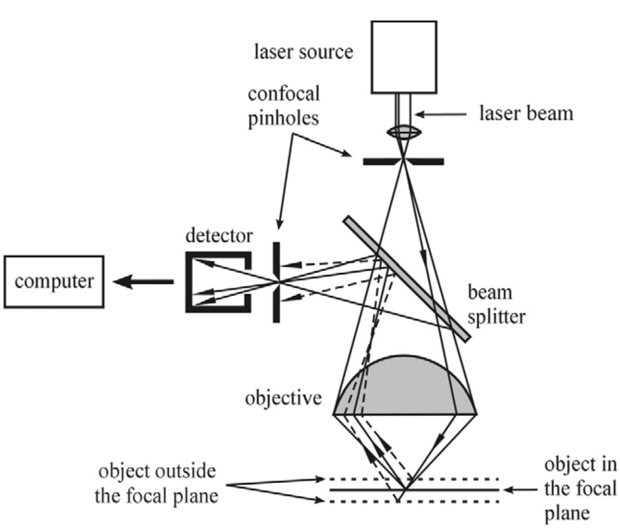

Fig. 1. Optical system of the LTS.

the automated perpendicular projections to the reference plane of several points of the three-dimensional map selected by the operator. The cup is defined as a part of the optic disc, that in the three-dimensional optic disc map corresponds to the area located in the depth equal or greater than the conventional value $\bar{h}$ – 50 μm below the reference plane. The introduced value $\bar{h}$ expresses the mean depth of the subsidiary area of the angular size 4° in the nasal part of the representative optic disc margin.

Method for the pallor analysis

In the case of the numerical description of the pallor, the ratio P/D of the representative pallor area and the representative total optic disc area were utilized. These representative areas were obtained using the suitable image analysis procedure of digital color optic disc images. Such images were found by the digital color video--camera of resolution 576×768 pixels connected with the adapted photographic system Retinofot Carl Zeiss Jena 201[6]. The actual size of the scanned area was approximately 5.8×4.4 mm. During every measurement, the photographic system mentioned above was located so that the rows of the acquired image matrix correspond to the horizontal direction. The brightness values of each of the corresponding three image color channels (i.e. red, green and blue) were standardly quantized to 256 discrete levels and represented by integers from 0 to 255. Value 0 represents the minimum (zero) brightness and value 255 represents the maximum brightness of each color channel.

The representative optic disc area of an image was manually demarcated by a convenient little excentric representative boundary ellipse, which connects five auxiliary points selected by the operator's experience in the used color digitized image of the optic disc OD. It was ascertained experimentally that the brightness G of the green color channel is optimal for the pallor determination[6]. The brightness G of the OD image generally undesirably depends on illumination of the OD during its photography and often inconveniently changes along the OD periphery. Hence, every considered brightness value $G(u, v)$ of the image point (u, v), located in the intersection of the u-th row and the v-th column of the image pixel array, was suitably normalized to the new value $G'_n(u, v)$ by the acceptable relation

$$G'_n(u,v) = \frac{2G(u,v)}{G_A + G_B} - G_{An} - \frac{G_{Bn} - G_{An}}{\bar{\nu}_B - \bar{\nu}_A}(\nu - \bar{\nu}_A) \qquad (1)$$

where

$$G_{An}(u,v) = \frac{2G_A(u,v)}{G_A + G_B}, \quad G_{Bn}(u,v) = \frac{2G_B(u,v)}{G_A + G_B} \qquad (2)$$

The introduced values G_A and G_B were defined as the green image channel brightness values of the largest occurrence in pixels of the referential areas A and B. The areas A and B mean the temporally and nasally located boundary parts of the representative OD area of the angle width 30° and of the thickness equal to the one fifth of the major semi-axis size a of the boundary ellipse (Figure

2). In this manner, the defined areas A, B are advantageously influenced minimally by the glaucoma progression. The also exploited quantities $\overline{v}_A$ and $\overline{v}_B$ represent the average values of column index v of pixels in the areas A and B.

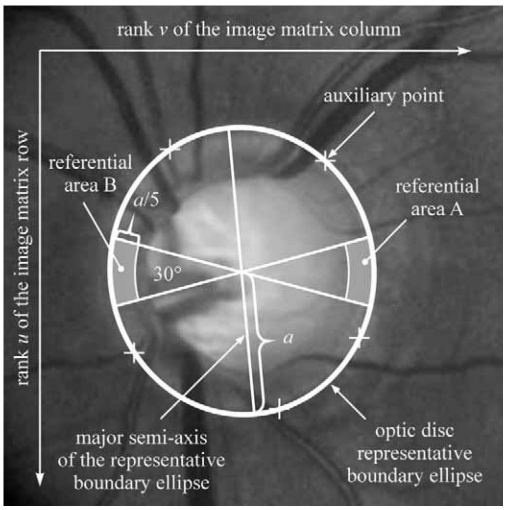

Fig. 2. The eye optic disc boundary ellipse and the referential areas A and B.

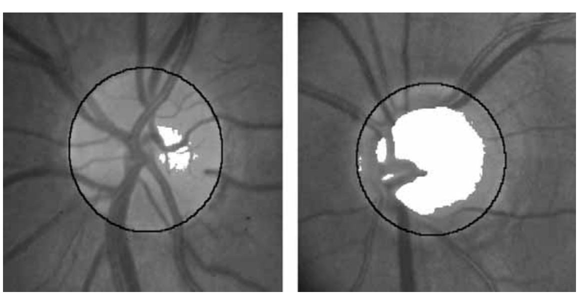

Fig. 3. Example of the healthy (left) and glaucomatous (right) OD image with the corresponding negligible small and expressive large bright pallor area. The boundary ellipses define the representative OD areas.

The simultaneously considered representative pallor area of the optic disc image is defined standardly as the image area within the representative boundary ellipse, where the normalized value G'_n is greater than or equal to the selected suitable threshold value p. The empirically established optimum value p=0.2 was accepted in our investigation. Figure 3 shows an example of healthy (left) and glaucomatous (right) OD image with the corresponding negligible small and expressive large bright pallor area. The outlined boundary ellipses define the representative OD areas.

Results and Discussion

All the considered 240 normal healthy and 240 glaucomatous eyes were investigated using both above-described methods. The C/D and P/D ratios were computed for the total optic disc of each investigated eye. Next, the histograms of obtained statistical occurrences (absolute frequencies) of C/D and P/D ratios were constructed in the case of normal healthy eyes and glaucomatous eyes (Figure 4 and Figure 5). The corresponding mean C/D values of normal healthy and glaucomatous eyes were 0.23 and 0.50 with the relevant standard deviation 0.12. In the case of statistical distributions of P/D, the mean value and standard deviation of normal healthy, respectively glaucomatous eyes were 0.10 and 0.07, respectively 0.24 and 0.09. The present results confirm the glaucoma influence on the considered P/D and C/D ratios. The diagnostic reliability of both introduced numerical parameters C/D and P/D can be determined and compared by the suitable normalized characteristic distance d of the relevant statistical distributions (histograms) for normal healthy and glaucomatous eyes, or using the relevant receiver operating characteristic (ROC) curves.

The required normalized distance d of statistical distribution of C/D or P/D is defined by the relation[6–8]

$$d = \frac{\left|\bar{t}_h - \bar{t}_g\right|}{\left[\dfrac{\sigma_h^2 - \sigma_g^2}{2}\right]^{1/2}} \tag{3}$$

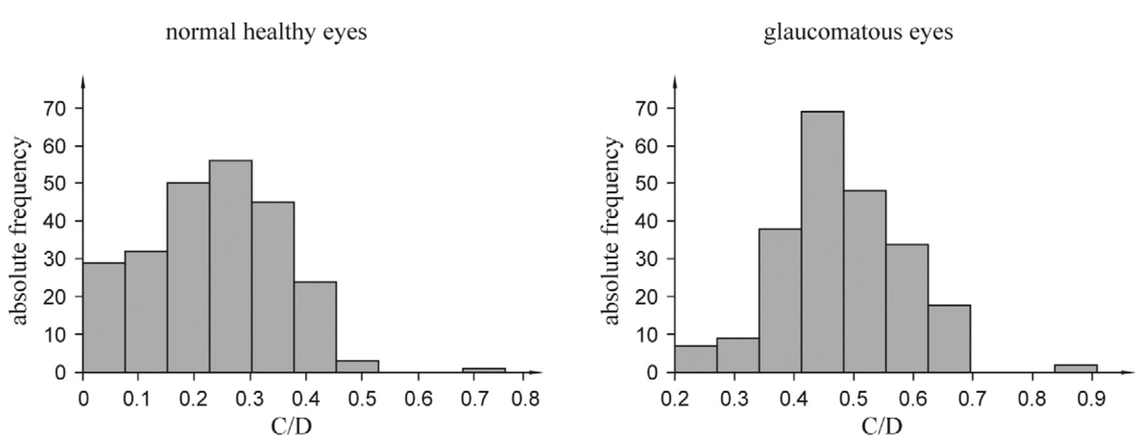

Fig. 4. The histograms of statistical distribution of C/D ratios in the case of normal healthy (left) and glaucomatous (right) eyes.

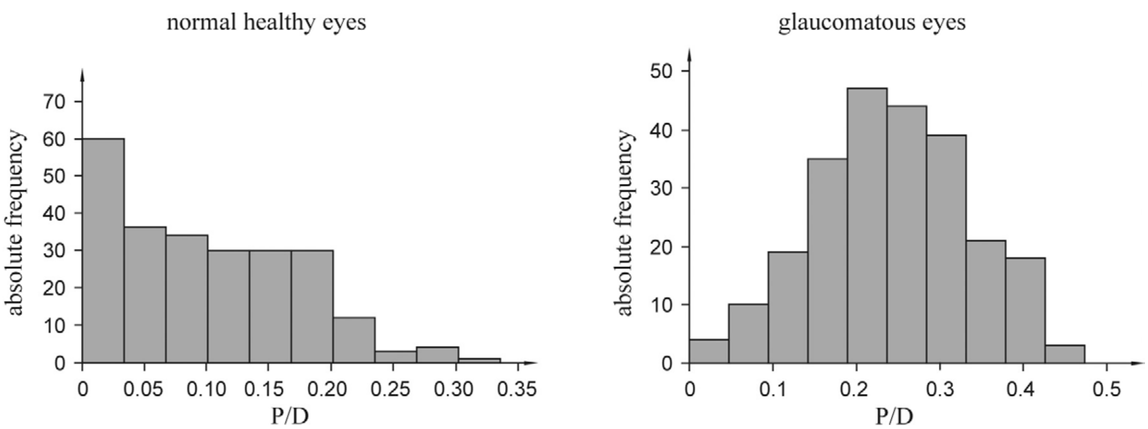

Fig. 5. The histograms of statistical distribution of P/D ratios in the case of normal healthy (left) and glaucomatous (right) eyes.

The introduced characteristic quantities $\bar{t}_h$, $\bar{t}_g$ and σ_h, σ_h represent the mean values and standard deviations of the statistical distributions of C/D or P/D, relating to healthy and glaucomatous eyes. The higher value of d indicates the higher diagnostic reliability. The values d = 2.19 and d = 1.73 were obtained for the C/D and the P/D ratios by our investigation.

An examined eye can be also diagnostically tested on the basis of comparison of its C/D or P/D ratio with a suitably chosen testing so-called cut-off value $t_{C/D}$ of C/D or $t_{P/D}$ of P/D. In such cases, the eye with the obtained numerical parameter C/D or P/D which is below, respectively over the chosen cut-off value is classified as healthy, respectively glaucomatous. For each value of $t_{C/D}$ or $t_{P/D}$, the described test also gives the relevant sensitivity (true positivity) and specificity[9]. The sensitivity is defined by the probability, that a real glaucomatous eye can be classified as glaucomatous. On the other hand, the specificity is equal to the probability, that a real healthy eye is classified as healthy. Moreover, the value of denotation (1-specificity) (perceived as false positivity) represents the probability of classification of a real healthy eye as glaucomatous. The dependence of sensitivity on (1-specificity) is known as the ROC curve[9]. The smoothed ROC curves (solid lines) relating to experimentally obtained data (dots) are plotted in Figure 6 for C/D and in Figure 7 for P/D. Their numerical comparison was conventionally carried out on the basis of area sizes under the relevant ROC curves. The larger area size means the better diagnostic reliability. The ascertained area sizes were 0.95 for C/D and 0.89 for P/D.

Conclusion

Two different methods of eye optic disc analysis were described and compared in this article with regard to

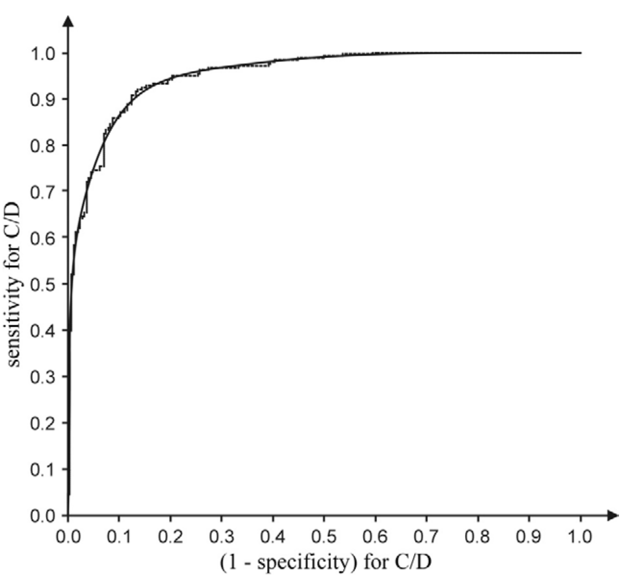

Fig. 6. The ROC curve in the case of C/D ratio approximated by the smooth curve (solid line) obtained using experimental data (dots).

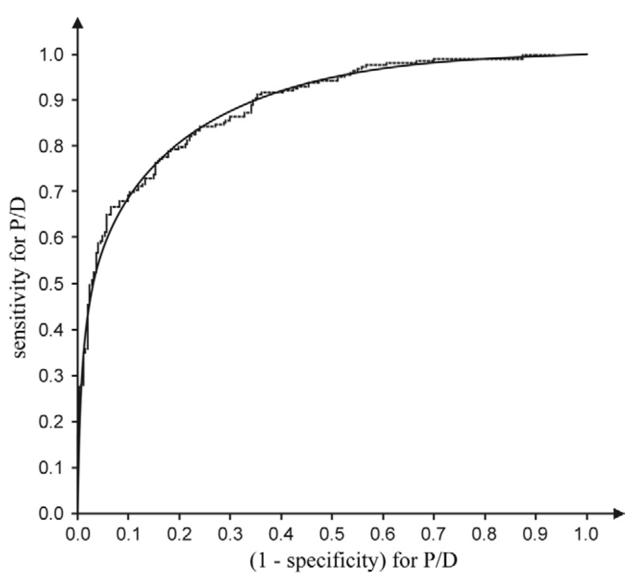

Fig. 7. The ROC curve in the case of P/D ratio approximated by the smooth curve (solid line) obtained using experimental data (dots).

glaucoma diagnostic. They relate to the analysis method of the cup of the optic disc using common laser scanning tomography and to the image analysis method of the optic disc pallor. The present cup analysis is based on creation and evaluation of the relevant three-dimensional map. Such a map was acquired by the laser scanning tomography. For the diagnostic purposes, the cup was numerically represented by the relative quantity (ratio) C/D. In the case of the pallor analysis, the color digital image of the optic disc was utilized. This image was processed using the proposed image analysis algorithm, which determines the relative numerical representation of the pallor area in the form of the P/D ratio. The verification and comparison of the diagnostic reliability of both C/D and P/D ratios were performed using the defined normalized distance of their statistical distributions and ROC curves. The present results show, that both ratios are significantly influenced by the glaucoma and can be effectively used in its diagnostics. It was also ratified that the designed pallor diagnostic analysis is less reliable than the diagnostic analysis of the cup. However, the advantage of the pallor analysis method consists in the possibility of its application to the color digitized computer images of the optic disc, which are obtainable by any currently available color fundus camera connected with a computer. In comparison with the laser scanning tomography, the designed pallor analysis method requires no other special devices.

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USPOREDBA POUZDANOSTI OPTIČKOG DISKA OKA I PODRUČJA BLJEDILA U DIJAGNOSTICI GLAUKOMA

SAŽETAK

Svrha ovoga rada bila je u dijagnostici glaukoma utvrditi pouzdanost dvaju parametara: veličinu relativne površine optičkog diska i relativnih područja bljedila. Oba parametra su mjerena na 240 zdravih očiju i 240 očiju s glaukomom. Rezultati su potvrdili da se oba parametra mogu upotrijebiti za dijagnosticiranje glaukoma. U dijagnostici glaukoma je analiza veličine relativnih područja bljedila manje pouzdana od analize veličine relativne površine optičkog diska.