CLINICAL INVESTIGATION

Feasibility Study on Computer-Aided Screening for Diabetic Retinopathy

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Abstract

Purpose: To conduct a feasibility study of computer-aided screening for diabetic retinopathy by developing a computerized program to automatically detect retinal changes from digital retinal images.

Methods: The study was carried out in three steps. Step 1 was to collect baseline retinal image data of 600 eyes of normal subjects with normal fundi and data of 300 eyes of diabetic patients with diabetic retinopathy. All data were recorded by digital fundus camera. Step 2 was to analyze all retinal images for normal and abnormal features. By this method, the automated computerized screening program was developed. The program preprocesses color retinal images and recognizes the main retinal components (optic disc, fovea, and blood vessels) and diabetic features such as exudates, hemorrhages, and microaneurysms. All of the accumulated information is interpreted as normal, abnormal, or unknown. Step 3 was to evaluate the sensitivity and specificity of the computerized screening program by testing the program on diabetic patients and comparing the program’s results with the results of screening by retinal specialists.

Results: Diabetic patients (182 patients, 336 eyes) were examined by retinal specialists; 221 eyes had a normal fundus and 115 eyes had nonproliferative diabetic retinopathy. Digital retinal images were taken of these 336 eyes and interpreted by the automated screening program. The program had a sensitivity and specificity of 74.8% and 82.7%, respectively.

Conclusions: The automated screening program was able to differentiate between the normal fundus and the diabetic retinopathy fundus. The program may be beneficial for use in screening for diabetic retinopathy. Further development of the program may provide higher sensitivity.

Key Words: diabetic retinopathy, digital image, screening

Introduction

Diabetic retinopathy is a leading cause of blindness in adults. In its early stage (nonproliferative diabetic retinopathy), it is evidenced as microaneurysms, retinal hemorrhages, hard exudates, venous dilatation, and cotton wool spots. After the disease progresses to proliferative diabetic retinopathy, laser photocoagulation can be performed to stop its progression. Screening for diabetic retinopathy is effective in reducing the incidence of blindness. A variety of screening methods for diagnosis and grading of diabetic retinopathy are used, such as direct and indirect ophthalmoscopy, slit-lamp binocular indirect ophthalmoscopy, and retinal photography. Nowadays, the use of digital cameras facilitates the processing of retinal photography. Images can be viewed immediately, and thus can be used when screening for diabetic retinopathy.

The purpose of this study was to determine the feasibility of computer-aided screening for diabetic retinopathy by developing a computerized program to detect diabetic
retinal changes from digital retinal images automatically. The automated screening program was evaluated by comparing its results with those from screening by retinal specialists.

Subjects and Methods

The study group from the Department of Ophthalmology, Siriraj Hospital, and the National Electronics and Computer Technology Center, Bangkok, carried out the project between March 2002 and March 2004. The study was divided into three steps.

Step 1

Step 1 was collection of baseline data from the Department of Ophthalmology. Data were recorded from 600 eyes of normal subjects with normal fundi and from 300 eyes of diabetic patients with diabetic retinopathy. The data were recorded by a Topcon TRC 500 IA digital fundus camera (Topcon, Tokyo Kagaku, Tokyo, Japan).

For all patients, their history of diabetic mellitus and general health conditions were recorded. Eye examinations included the Snellen chart visual acuity test, tonometry, pupil dilation and fundus examination by direct or indirect ophthalmoscopy, and slit-lamp biomicroscopy with a +90 dioptre lens.

Retinal images of the normal fundus of the 600 eyes from the 339 non-diabetic subjects and of the 300 eyes of the 154 diabetic patients with non-proliferative diabetic retinopathy were recorded by a digital fundus camera. A single image, a 50° field centred on the macula, of each eye was obtained. All images were of sufficient quality to show retinal detail. The exclusion criteria for the study were diabetic patients with other associated retinal diseases or proliferative diabetic retinopathy, and patients who had previously received laser photocoagulation.

Step 2

In step 2, all retinal images were analysed for normal fundus features and abnormal findings in the early stage of diabetic retinopathy. The automated computerized screening program for diabetic retinopathy was developed by the National Electronics and Computer Technology Center (NECTEC), Bangkok, Thailand.

The program was designed to differentiate between the features of a normal fundus and the abnormal findings characteristic of the early stage of diabetic retinopathy, such as hard exudates, cotton wool spots, microaneurysms, and retinal haemorrhages. The program proceeded as follows:

1. Colour retinal images were preprocessed by applying a local contrast enhancement technique. Digital images were obtained with a resolution of 570 x 550 pixels, with 256 grey levels for each red, green, and blue pixel element. Normally, the quality of the contrast at the centre of the retinal images was high and then diminished towards the periphery. Therefore, the preprocessing technique was applied to minimize this effect, thus producing a more uniform image.

2. The main retinal main components (optic disc, fovea and blood vessels) were recognized by identifying the location, variation in intensity, and continuity of the vascular structure. The optic disc was recognized as the area with the highest variation in intensity among adjacent pixels. Blood vessels were identified by means of a multilayer perceptron neural network, the inputs of which were derived from a principal component analysis of the image and edge detection of the first principal component. The fovea was located using matching correlation.

3. Diabetic features such as exudates, retinal haemorrhages, and microaneurysms were recognized. A recursive region growing segmentation algorithm was used for exude recognition. Haemorrhages were recognized by colour and template matching. To avoid misclassification, the blood vessels identified by the neural network technique were extracted from the image.

4. All the information was accumulated and interpreted as normal, abnormal, or unknown.

The computerized screening program was loaded into the computer hardware. The fundus of the patient was recorded by a digital retinal camera. Then the retinal image was transferred to the computerized screening program, and the program interpreted the image as normal, abnormal, or unknown (Fig. 1).

The program interpreted the image as normal if there was no abnormal finding, and it interpreted it as abnormal if retinal haemorrhages, microaneurysms, or exudates were detected. If the image was not clear enough to be interpreted, the program read it as unknown (Figs 2, 3).

Step 3

In step 3, the computerized screening program was evaluated for sensitivity and specificity by testing a new group of subjects and comparing the results with those from screening by retinal specialists.

A new group of 182 diabetic patients were examined by retinal specialists. No diabetic retinopathy was found in 116 patients, and there were 66 cases of diabetic retinopathy. Patient age ranged from 17 to 85 years. Five had diabetes mellitus type 1 and 177 had type 2. The mean duration of diabetes was 10.02 ± 6.84 years.

This group of patients was sent for digital retinal photography. Digital retinal photographs could be taken of only 336 eyes (221 eyes with normal fundus and 115 eyes with non-proliferative diabetic retinopathy, as diagnosed by retinal specialists), and these eyes were tested by the screen-
Figure 1. Process of automated screening program development. Accumulated data are used to judge whether the fundus is a normal retina or the retina of a patient with diabetic retinopathy.

Figure 2. Screening program on computer screen. The program is judging the retina as “normal” because there is no abnormal finding.
ing program. The remaining 28 eyes had ocular media opacity from cataract, so fundus pictures could not be obtained. The data collected for this group of patients were analysed with SPSS software (SPSS, Chicago, IL, USA).

Results

Of the 221 eyes of diabetic patients with normal fundi, as confirmed by retinal specialists, the screening program interpreted 167 eyes as normal, 35 as abnormal, and 19 as unknown. Of the 115 eyes with diabetic retinopathy, the program interpreted 27 as normal, 80 as abnormal, and 8 as unknown (Table 1).

In the diabetic test group of 336 eyes, 27 eyes (8.03%) could not be analysed by the computerized screening program and were interpreted as unknown. Of the 309 eyes that could be analysed by the program, 80 were true positives, 35 were false positives, 167 were true negatives, and 27 were false negatives. Sensitivity was defined as the ratio of true positives to (true positives + false negatives). Specificity was defined as the ratio of true negatives to (true negatives + false positives). Thus, the automated screening program showed a sensitivity of 74.8% and a specificity of 82.7% (Table 2). Screening by the automated screening program and by retinal specialists can differentiate between the normal fundus and diabetic retinopathy with statistical significance ($P < 0.001$).

### Table 1. Interpretation of retinal changes by automated screening program and retinal specialist

<table>
<thead>
<tr>
<th>Retinal specialist’s interpretation</th>
<th>Program interpretation (no. of eyes)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td>No diabetic retinopathy (221 eyes)</td>
<td>167</td>
</tr>
<tr>
<td>Diabetic retinopathy (115 eyes)</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>194</td>
</tr>
</tbody>
</table>

### Table 2. Sensitivity and specificity of automatic screening program

<table>
<thead>
<tr>
<th>Screening test result (automated program)</th>
<th>Diabetic retinopathy (retinal specialist)</th>
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</thead>
<tbody>
<tr>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>80</td>
<td>35</td>
</tr>
<tr>
<td>27</td>
<td>167</td>
</tr>
<tr>
<td>Total</td>
<td>107</td>
</tr>
</tbody>
</table>

Sensitivity 74.8%; specificity 82.7%; positive predictive value = 80/115 = 69.56%; negative predictive value = 167/194 = 86.08%. $\chi^2$ squared test, $P < 0.001$; kappa statistic, 0.564.
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The positive predictive value (PPV) was 69.56% (the probability that a patient with a positive test result had diabetic retinopathy), and the negative predictive value (NPV) was 86.08% (the probability of a patient with a negative screening test result truly not having diabetic retinopathy).

Agreement between the interpretation by the computer-aided screening program and the retinal specialist was evaluated using the Kappa statistic (k). The quality of agreement is graded as poor (k < 0.04), fair (0.41–0.69), or good (0.70–1.00). In this study, k was 0.564, representing fair agreement.20

**Discussion**

A variety of methods are used to screen for diabetic retinopathy. The sensitivity of detection of diabetic retinopathy depends on the experience of the tester and the method of testing. Susman et al.7 showed that examination of diabetic patients with direct ophthalmoscopy by internists, senior medical residents, and diabetologists had a sensitivity of diagnosis of proliferative diabetic retinopathy averaging 49 ± 5%. General ophthalmologists and retinal specialists using direct and indirect ophthalmoscopy had a sensitivity of 96 ± 2%, whereas retinal specialists never failed to diagnose correctly proliferative diabetic retinopathy.

Taking retinal photographs of seven 30° fields in stereoscopic view is the standard procedure for determining the presence and severity of diabetic retinopathy.21 Obtaining seven stereo pairs for each eye is time-consuming, but if the photographic field is reduced to four fields, the sensitivity in the grading of diabetic retinopathy is reduced by 5%.2 In screening for diabetic retinopathy, when ophthalmoscopy is combined with retinal photography, the sensitivity of detecting diabetic retinopathy increases. O'Hare et al.23 reported that the sensitivity of screening by general practitioners and opticians for referable retinopathy with ophthalmoscopy was 65%, and improved to 84% with retinal photographs.

Nowadays, advanced digital camera systems make the photographic process easier. Digital retinal photography can be used to screen for diabetic retinopathy in a large population. Many types of digital retinal cameras are available; a camera that can capture a wide field of 45°–50° makes possible a higher sensitivity for the detection of retinal changes. Recent studies suggest that single-field photography centred on the macula may be adequate for diabetic retinopathy screening. The sensitivity for detecting sight-threatening retinopathy is similar between single- and multiple-field photography.24 25

Some investigators have used advanced computer programming techniques to develop programs for automatic detection of retinal changes. Automated detection of retinal exudates, haemorrhage, and microaneurysms can be used in screening for diabetic retinopathy.26 27 The automated screening program in this study was developed by obtaining images of normal Asian fundus and fundi with nonproliferative diabetic retinopathy. The computer program was then taught to recognize the normal structures of the fundus, such as the optic disc, blood vessels, and fovea, and to distinguish them from abnormal features of diabetic retinopathy, such as exudates, microaneurysms, and haemorrhages using these images.

In this study, we did not grade the abnormal findings by severity, such as massive retinal haemorrhages or exudates in the macular area. The aim was only to distinguish normal features from abnormal features reflecting diabetic retinal changes. The program was tested and evaluated by comparing its results with the results of examinations by retinal specialists. The effectiveness of the automated screening program is shown by its sensitivity and specificity. In general, a screening test should be sensitive enough to detect the disease and specific enough to exclude non-affected individuals. Our study showed that the screening program had a sensitivity of 74.8% and a specificity of 82.4%. False negatives occurred when patients were in the early stages of diabetic retinopathy, as some minute microaneurysms could not be detected by the program. False positives occurred under certain conditions: (1) if there was reflection of the flashlight from the retina or from the margin of the pupi, then the high intensity of the image could be misinterpreted as the optic disc or as exudates; (2) the program could not differentiate drusen of the retina from hard exudates; and (3) a red foveal colour could be misinterpreted as a foveal haemorrhage.

The program was unable to interpret the images of patients with opacity of the lens, which obscured the details of the retina, or of highly myopic patients with a sceral crescent, which caused very high reflectivity. Although the sensitivity of the automated program in this study was only 74.8%, it is still worthwhile for use in clinical practice to detect diabetic retinopathy. Javitt et al.28 suggested that a sensitivity of 60% or greater maximized cost effectiveness when screening for diabetic retinopathy.

This study showed some limitations of automated screening programs:

1. When screening by digital retinal photography, the ocular media of the patient must be clear enough to show retinal detail.
2. The pupil should be dilated during the screening process in order to obtain a good quality picture and a larger field.
3. Diabetic patients with drusen or high myopia with a myopic crescent may have incorrect results.
4. The program is not sensitive enough to detect the early changes of nonproliferative diabetic retinopathy.

In conclusion, this study showed that the automated screening program was able to differentiate between a normal fundus and a fundus showing features of diabetic retinopathy. It should be beneficial for use in screening for diabetic retinopathy. The program reduces the clinician's workload, and the retinal image can be interpreted immediately. The program needs further technical development to gain higher sensitivity and specificity. An effective
program should be developed for patients with nondilated pupils. In the future, this program might be of benefit for use in a mobile unit, and when combined with ophthalmoscopy, it can improve the sensitivity of diabetic retinopathy screening.

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References