

Automated detection of diabetic retinopathy on digital fundus images

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Abstract

Aims The aim was to develop an automated screening system to analyse digital colour retinal images for important features of non-proliferative diabetic retinopathy (NPDR).

Methods High performance pre-processing of the colour images was performed. Previously described automated image analysis systems were used to detect major landmarks of the retinal image (optic disc, blood vessels and fovea). Recursive region growing segmentation algorithms combined with the use of a new technique, termed a 'Moat Operator', were used to automatically detect features of NPDR. These features included haemorrhages and microaneurysms (HMA), which were treated as one group, and hard exudates as another group. Sensitivity and specificity data were calculated by comparison with an experienced fundoscopist.

Results The algorithm for exudate recognition was applied to 30 retinal images of which 21 contained exudates and nine were without pathology. The sensitivity and specificity for exudate detection were 88.5% and 99.7%, respectively, when compared with the ophthalmologist. HMA were present in 14 retinal images. The algorithm achieved a sensitivity of 77.5% and specificity of 88.7% for detection of HMA.

Conclusions Fully automated computer algorithms were able to detect hard exudates and HMA. This paper presents encouraging results in automatic identification of important features of NPDR.

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Keywords image analysis, image recognition, neural network, diabetic diagnosis, retinopathy

Introduction

The benefits and cost-effectiveness of screening for diabetic retinopathy are well recognized [1–3] but screening services in the UK remain incomplete [4]. Growing numbers of diabetic patients will increase the pressure on available infrastructure and resources. A WHO collaborative study projected that by 2010 there would be over 3 million diabetic patients in the

UK, while the global diabetic burden is expected to increase between 1995 and 2010 from 118 to 221 million people [5].

Screening in the UK is by fundal examination performed by medical or optometric staff or by observation of various photographic methods. In those units using photography, trained personnel are required to screen the retinal images. A screening method that does not require trained personnel would be of great benefit to screening services by decreasing their costs. A wholly automated approach involving computer analysis of fundus images could provide an immediate classification of retinopathy without the need for specialist opinions.

There has been significant recent interest in the development of a national screening strategy for diabetic retinopathy [6]

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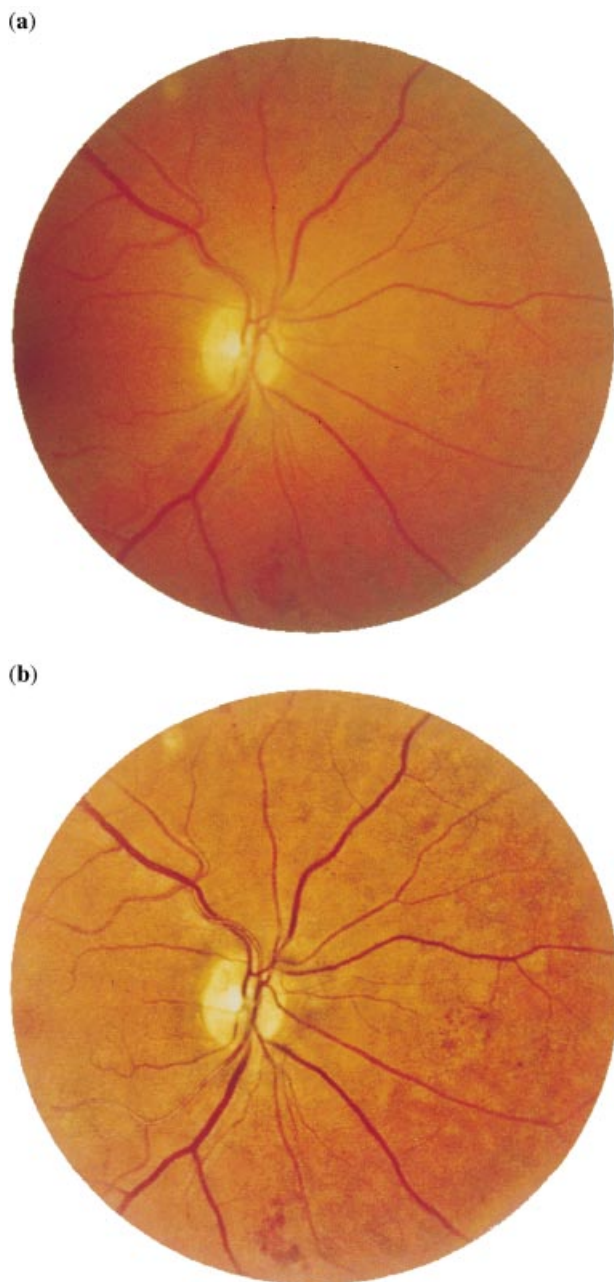


Figure 1 Colour contrast enhancement. (a) Original digital colour retinal image. (b) Retinal image after pre-processing by local colour contrast enhancement.

and, while no consensus currently exists on the optimal method of screening, digital recording of fundus images is one of the options under consideration and is already in use in many centres. Digital images have been shown to be superior to Polaroid in terms of image quality [7] and comparable to 35-mm film [8]. Compressed digital image files are also amenable to data transfer for telescreening and for storage in databases. The availability of retinal images from screening programs in digital form would make automated analysis a cost-effective and logical next step [9].

In this paper we describe our progress in the development of an automated system for screening of diabetic retinopathy. We have previously described a system which first pre-processes the images to improve quality and reduce artefacts [10]. A variety of methods was employed for the detection of the major landmarks on a retinal image—the optic disc, blood vessels and fovea. In this study, automated computer-based algorithms were used to recognize important features of non-proliferative diabetic retinopathy (NPDR), namely microaneurysms, haemorrhages and hard exudates.

Methods

One hundred and twelve digital fundal images (45° field) of patients attending a diabetic retinopathy screening service were captured using a Topcon TRC-NW5S non-mydratic camera and stored as tagged image format (tiff) files. The patient's pupils were routinely dilated at the screening service with Tropicamide 1%. Thirty images of the posterior pole in which haemorrhages, microaneurysms or exudates were present were selected for analysis.

Our method for automatic diabetic retinopathy screening involved three successive sequences: first, pre-processing of the colour image; second, identification of the main retinal components [9]; finally, recognition of diabetic retinopathy lesions.

Pre-processing of colour retinal images

Digital images were obtained at a resolution of 570×550 with 256 grey levels for each red, green, blue pixel element. A typical digital colour fundal image is shown in Fig. 1a. Contrast at the centre of retinal images tended to be of good quality but diminished towards the periphery. A pre-processing technique was applied to minimize this effect, thus producing a more uniform image. We have described this work in detail elsewhere [9] and shall summarize it as follows.

Consider the three primary colours Red, Green, and Blue, which represent the RGB colour model. In our analysis, the RGB components of an image were transformed to an Intensity, Hue, Saturation (IHS) model. Adaptive, local, contrast enhancement was applied to the intensity band and the subsequent image was converted back to RGB for display. The effect of pre-processing Fig. 1a is shown in Fig. 1b.

Recognition of main retinal components

As previously described, the main features of a fundal image were defined as the optic disc, fovea and blood vessels. In brief, the optic disc was recognized by identifying the area with the highest variation in intensity of adjacent pixels. Blood vessels were identified by means of a multilayer perceptron neural network [11–14] for which inputs were derived from a principle component analysis of the image and the edge detection of the first principle component. With a limited search space around the optic disc, the fovea was located using matching correlation [15]. Recognized fundal components are shown in Fig. 2.

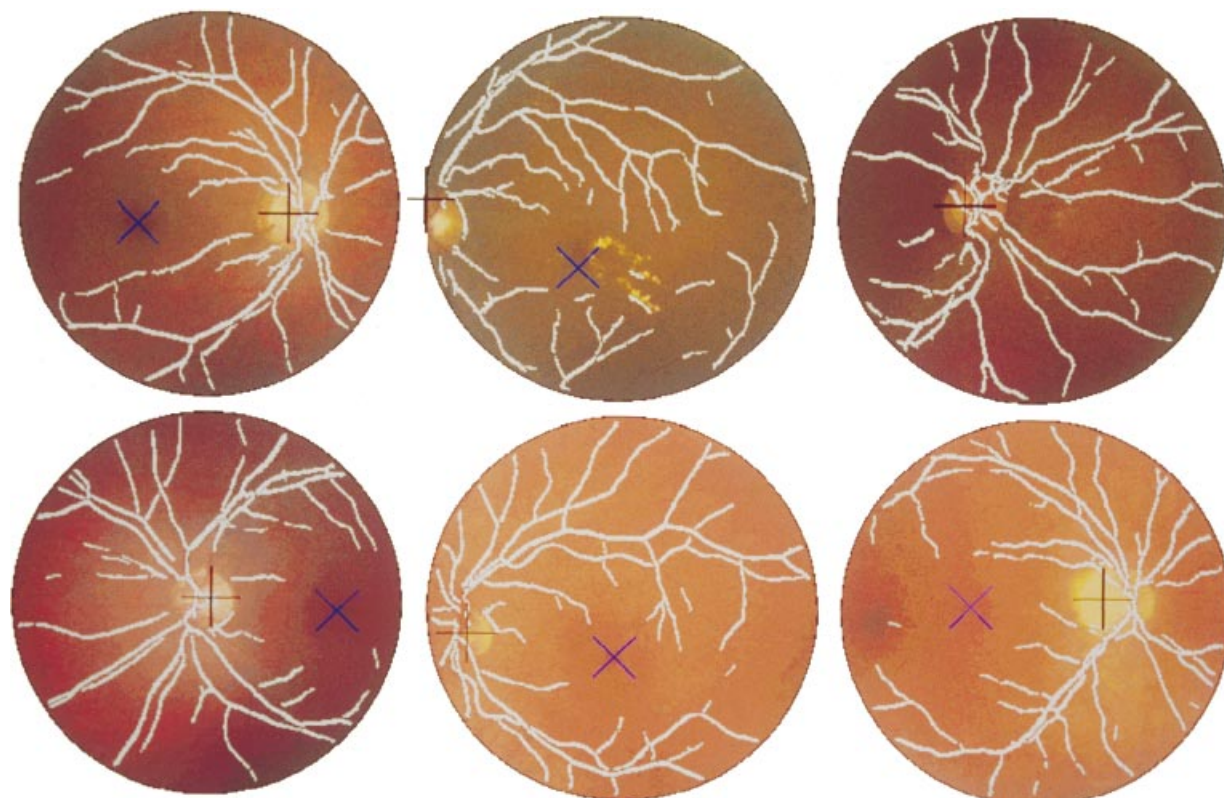


Figure 2 Recognition of main components of fundus images are represented by the following: white, vessels; black plus (+), optic disc; blue cross (x), fovea.

Recognition of diabetic retinal lesions

Retinal lesions to be identified were defined as hard exudates, haemorrhages and microaneurysms. There is a racial variation in fundal colour. Retinal images tend to be red-orange in Caucasians and dark purple in African Caribbeans. In this work the data set was predominantly Caucasian. To avoid confusion when the algorithms were applied, all retinal images were adjusted to a red-orange standard (Fig. 3).

Recognition of hard exudates

Exudates were defined as yellow lesions of various shapes and size with relatively distinct margins. A recursive region growing segmentation (RRGS) algorithm was used for exudate detection. The basis of RRGS is the identification of similar pixels within a region to determine the location of a boundary. To establish if two adjacent pixels are similar they must satisfy some criterion such as grey level or colour. In RRGS, adjacent pixels within the same region are considered to have fairly homogeneous grey scale properties.

Consider each pixel of the image in raster order. A pixel p , at co-ordinates (x, y) has four neighbouring pixels orientated above, below, left and right with co-ordinates $(x, y + 1)$, $(x, y - 1)$, $(x - 1, y)$ and $(x + 1, y)$, respectively. Consider an adjacent pixel p_i , where i is the vertical or horizontal co-ordinate relative to p . The first step of the algorithm was to calculate the difference in intensity between p and p_i . If the difference was less than or equal to a threshold value of 10, then p_i was added

to the region and set to p . The process was repeated until all pixels considered for merging and the original pixel comprised a region. The median intensity of the region was calculated and replaced the original intensity of the merged pixels. The cycle was repeated until the whole image was segmented. Figure 4b is the segmented image of the original shown in Fig. 4a.

By using thresholding, a binary image was produced from which an exudate mask was created as follows.

Consider the segmented image (Fig. 4b) which comprises exudate and non-exudate regions. The median intensity of the 'background' (defined as the region with the most pixels) was set as the threshold value for classification of the image. Segmented regions above this threshold were set to intensity 255 (white) and classified as exudate regions. Segmented regions below the threshold were set to intensity 0 (black) and classified as non-exudate regions. As the optic disc was a similar colour to that of exudates with a well-defined boundary, it was extracted from the image using the position recognition algorithm (as described previously) to avoid classification with the exudates. Finally, the exudate mask (with the exudates depicted as blue regions) was overlaid onto the original image as shown in Fig. 4c. Figure 5 demonstrates further examples of exudate recognition.

Recognition of haemorrhages and microaneurysms

Microaneurysms were defined as small, round, red dots whilst haemorrhages had 'dot', 'blot' or 'flame' configurations. The lesions are the same colour as blood vessels and very similar in

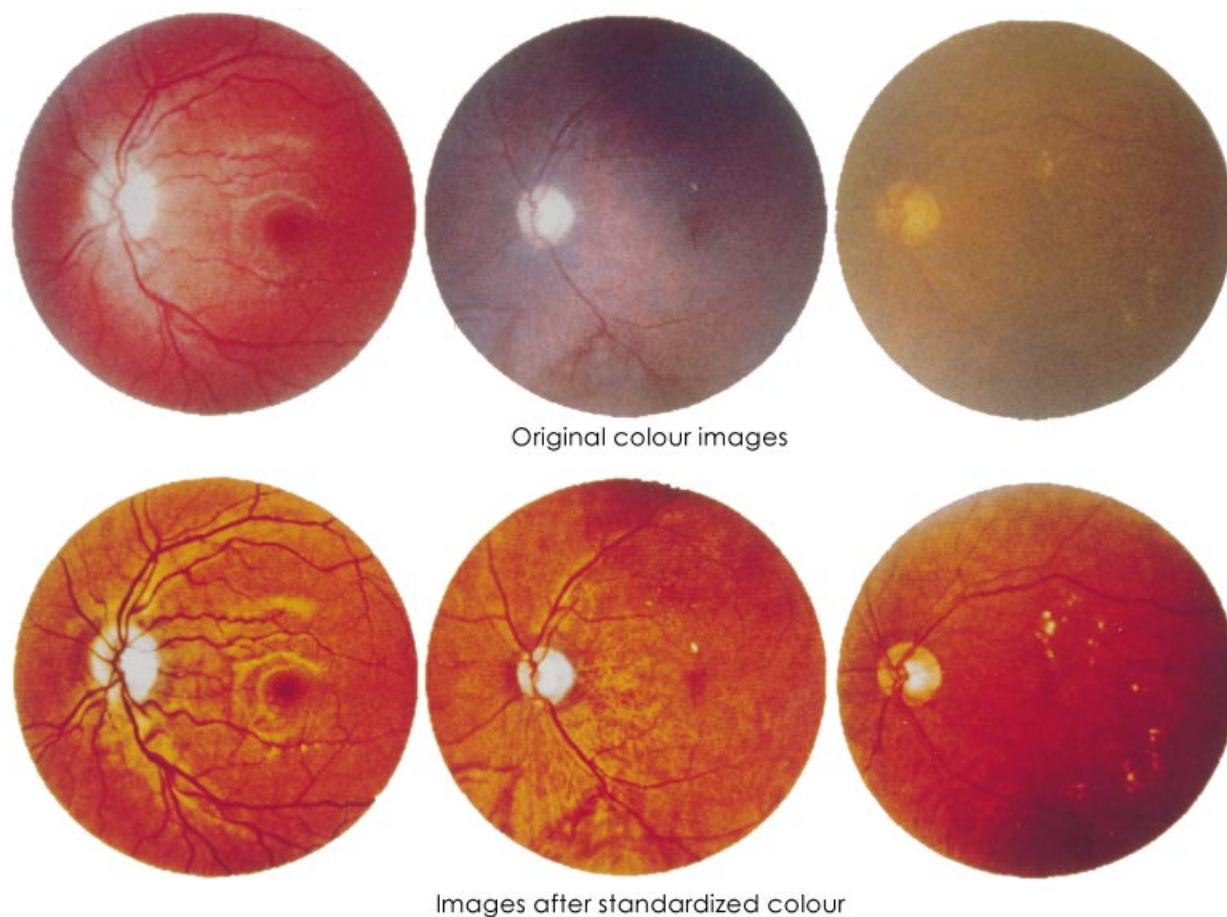


Figure 3 Standardized colour fundus images.

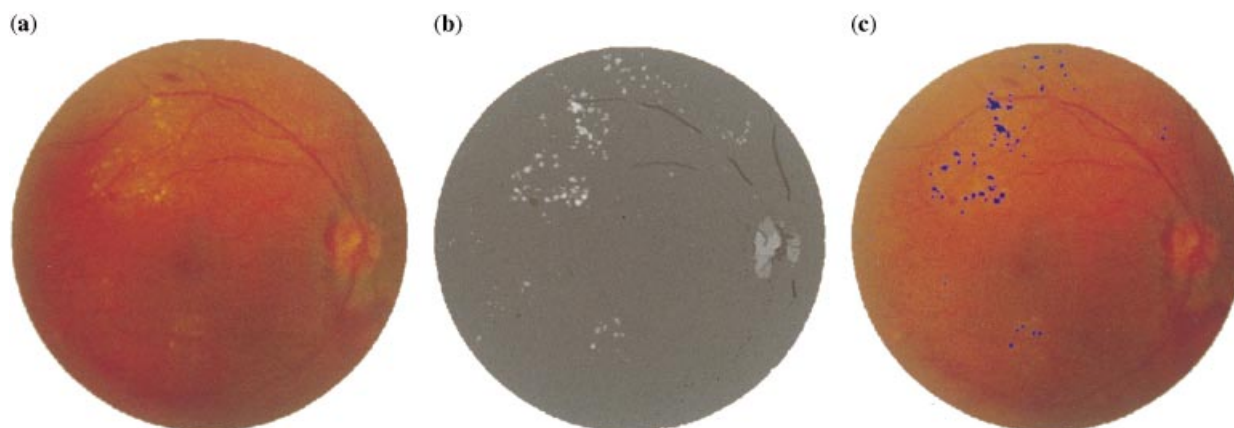


Figure 4 Procedure for exudate recognition. (a) Original colour image. (b) Classification of image by recursive region growing segmentation. (c) Result of exudate recognition.

colour to the fundal background. The colour band chosen for recognition of haemorrhages and microaneurysms (HMA) was green as it contained more information and greater contrast for red features. In order to sharpen the edges of the red lesions against the red-orange background, a 'Moat Operator' was applied

(see Appendix, which can be found on the *Diabetic Medicine* Website at <http://www.blackwell-science.com/products/journals/suppmat/DME/DME613/DME613sm.htm>). Figure 6b shows the result of applying the Moat Operator to Fig. 6a. RRGs and thresholding was used to classify the image into HMA

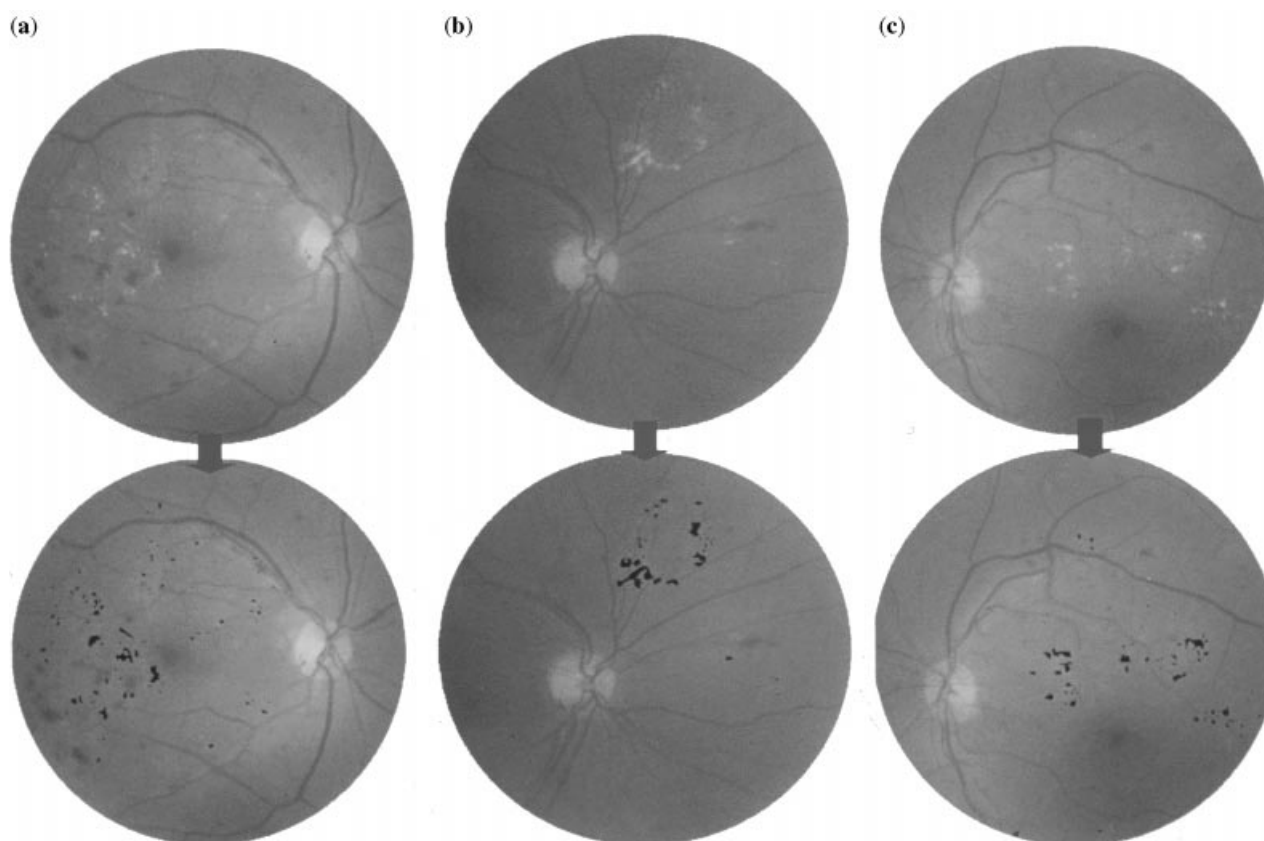


Figure 5 Further examples of exudate recognition.

and non-HMA regions. Due to similarities in colour, the blood vessels were classified into the same group as HMA (Fig. 6c). To overcome this problem, a neural network (NN) technique was used to identify the blood vessels and extract them from the image (Fig. 6d,e). The final HMA mask was overlaid onto the original image as shown in Fig. 6f.

Validation of diabetic retinopathy recognition

In order to establish the accuracy with which the algorithms were able to detect diabetic lesions, an experienced ophthalmologist (H.L.C.) was used as a reference standard. A 10×10 pixel grid was overlaid onto the original image containing exudates and HMA. The ophthalmologist was asked to fill in manually areas of the grid containing lesions. The appropriate algorithm was applied and a direct comparison was made with regions identified by the ophthalmologist (Fig. 7).

Results

The algorithm for exudate recognition was applied to 30 retinal images of which 21 contained exudates and nine were without pathology (Table 1). The sensitivity and specificity for exudate detection were 88.5% and 99.7%, respectively.

HMA were present in 14 retinal images (Table 2). The algorithm achieved a sensitivity of 77.5% and specificity of 88.7% for detection of HMA when compared with the ophthalmologist.

Table 1 Results for the detection of exudates

	Segments classified as exudates	Segments classified as normal
Exudates	793	100
Normal	167	59 720

Table 2 Results for the detection of haemorrhages and microaneurysms

	Segments classified as haemorrhages and microaneurysms	Segments classified as normal
Haemorrhages and microaneurysms	787	228
Normal	3343	26 227

Discussion

In this study, computer-based algorithms were used to pre-process retinal digital images, localize the major retinal landmarks and recognize diabetic pathologies, without any intervention from an operator. We have previously described a variety of techniques employed in image pre-processing and identification of the optic disc, fovea and retinal blood vessels [9]. This study has added to the previous work by showing that it is

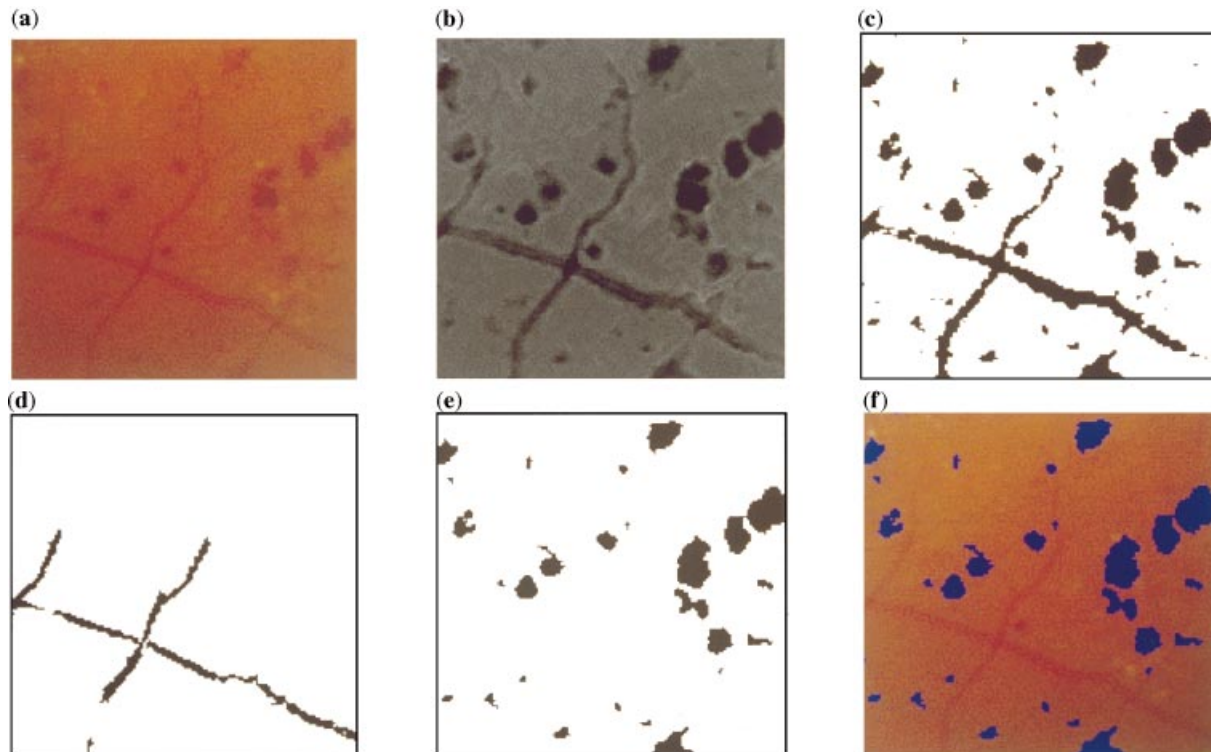


Figure 6 Procedure for haemorrhage and microaneurysm (HMA) recognition. (a) Original subimage, size 140×140 pixels. (b) Image after application of the Moat Operator. (c) Classification of image by recursive region growing segmentation. (d) Classification of image into vessels and non-vessels by artificial neural networks. (e) Vessel regions removed from image. (f) HMA mask overlaid onto original image.

possible to use recursive region growing segmentation algorithms to recognize hard exudates, haemorrhages and microaneurysms. A new algorithm, termed a 'Moat Operator', was used to optimize recognition of haemorrhages and microaneurysms.

Recognition of hard exudates was high, with only faint exudates not identified. The detection of haemorrhages and microaneurysms was a more difficult task. Further work will be required to improve the detection accuracy of these red-coloured lesions, which may be confused with segments of small retinal blood vessels. In addition, haemorrhages adjacent to blood vessels were not identified by the algorithm.

The accurate assessment of pathologies using the smallest sampling areas (pixel by pixel) was not possible by the clinician, so 10×10 pixel grids were overlaid upon the original image for the purposes of localizing lesions. Each of the squares on the grid constituted a sampling unit. The number of control areas of normal retina was high because only small areas of the image are affected by pathology in most diabetic retiniae. The subjective nature of the assessment by the human observer will have introduced error, but we felt that an approximate accuracy of pathology recognition could be determined.

The sensitivity and specificity of recognition of lesions of diabetic retinopathy were comparable to other methods of automated screening for analysis of digital images. Gardner *et al.* described an automated computerized method for detecting diabetic retinopathy using artificial neural networks (ANNs)

[16]. His detection rates for hard exudates using ANNs were 93.1% for both sensitivity and specificity, while this study showed sensitivity and specificity of 88.5% and 99.7%, respectively. His detection rates for haemorrhages were 73.8% for both sensitivity and specificity, while sensitivity and specificity for haemorrhages and microaneurysms in this study were 77.5% and 88.7%, respectively.

The results from our study and that of Gardner *et al.* are not directly applicable to the clinical situation because the sensitivity and specificity data only relate to the detection of individual lesions on an image. The results are not a comparison of the clinical situation for which the sensitivity and specificity results would be required by eye or patient. Furthermore the images, although taken from a screening service, have been selected for the presence of features and therefore are not a good representation of those that would be seen in a screening population. However, both studies provide an indicator of the capability of automated detection in diabetic retinopathy.

British Diabetic Association guidelines recommend a minimum standard of 80% sensitivity and 95% specificity of detection of sight-threatening diabetic retinopathy by any method [17]. In their health policy model, Javitt *et al.* suggested that a sensitivity of 60% or greater maximized cost-effectiveness in screening for diabetic retinopathy [18]. Increasing screening sensitivity from 60% to 100% provided little additional benefit due to the frequency of screening and the likelihood that

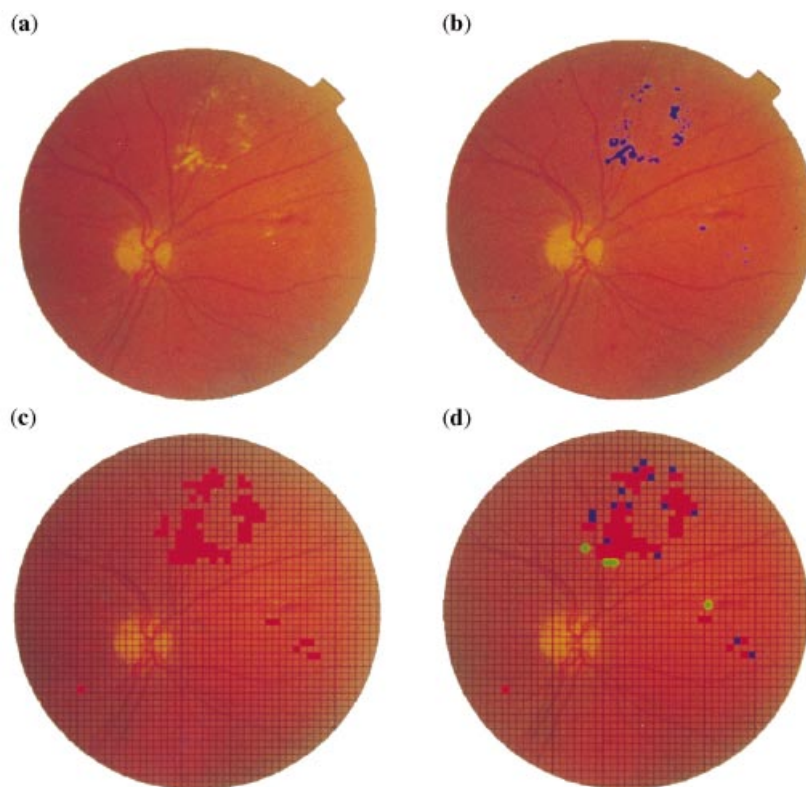


Figure 7 Statistical validation procedure for hard exudate recognition. (a) Original retinal colour image. (b) Hard exudate recognition. (c) 10×10 pixel grid overlaid onto original retinal colour image with position of hard exudates filled in by clinician. (d) Comparison between grid mask completed by clinician and computer algorithm, where red indicates exudate regions identified by both clinician and algorithm, green represents areas mistaken as exudates by algorithm and blue represents exudate regions identified by clinician but not by algorithm.

retinopathy cases missed at one visit will be detected at the next. The early results presented here compare favourably with these guidelines in terms of recognition of individual lesions. At this stage, the system analyses on a pixel by pixel basis and does not provide analysis of the complete image. This would be required if the system is required to grade retinal images. Future work will include attempts to recognize sight-threatening maculopathy, e.g. the software is able to correctly identify the fovea in 84.5% of cases (9) and there is potential to superimpose a perifoveal mask to examine for hard exudates in this area.

It will be technically difficult to develop a reliable automated system for detection of diabetic retinal neovascularization. This may be a major stumbling block to the implementation of software-based grading of sight-threatening retinopathy, unless one implies a certain level of peripheral retinal ischaemia from the widespread presence of other retinal lesions. The first step therefore is to develop and validate a system that provides a reliable yes–no answer to the question of whether any diabetic retinopathy is present. Validation will need to include images that contain non-diabetic retinal pathology to assess if these can be discriminated by the software. A threshold sensitivity for referral would need to be incorporated to allow for false positives. Development of a reliable screening system, which provides a simple yes–no answer, may be enough to reduce diabetic screening requirements by trained personnel by up to 70%.

In conclusion, this progress study presents encouraging results in identification of important features of background diabetic retinopathy. The automated computer algorithms were

shown to have good levels of accuracy in recognition of lesions when compared with an experienced fundoscopist. Further investigation is required to recognize the presence of perifoveal exudates and to validate the system's ability to discriminate the presence or absence of retinopathy.

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References

- 1 Javitt JC, Aiello LP, Chiang Y, Ferris FL, Canner JK, Greenfield S. Preventative eye care in people with diabetes is cost-saving to the federal government: implications for health-care reform. *Diabetes Care* 1994; 17: 909–717.
- 2 Diabetes care and research in Europe: the St Vincent Declaration. *Diabet Med* 1990; 7: 360.
- 3 British Diabetic Association. *St Vincent Joint Task Force for Diabetes. Final Report*. London: British Diabetic Association, 1995.
- 4 Bagga P, Verma D, Walton C, Masson EA, Hepburn DA. Survey of diabetic retinopathy screening services in England and Wales. *Diabet Med* 1998; 15: 780–782.
- 5 Amos AF, McCarty DJ, Zimmet P. The rising global burden of diabetes and its complications: estimates and projections to the year 2010. *Diabet Med* 1997; 14: S7–13.

- 6 Hart PM, Harding S. Is it time for a national screening programme for sight-threatening diabetic retinopathy? *Eye* 1999; **13**: 129–130.
- 7 Ryder REJ, Kong N, Bates AS, Sim J, Welch J, Kritzing EE. Instant electronic imaging systems are superior to Polaroid at detecting sight-threatening diabetic retinopathy. *Diabet Med* 1998; **15**: 254–258.
- 8 George LD, Halliwell M, Hill R, Aldington SJ, Lusty J, Dunstan F, Owens DR. A comparison of digital retinal images and 35 mm colour transparencies in detecting and grading diabetic retinopathy. *Diabet Med* 1998; **15**: 250–253.
- 9 Sinthanayothin C, Boyce JF, Cook HL, Williamson TH. Automated localization of the optic disc, fovea, and retinal blood vessels from digital colour fundus images. *Br J Ophthalmol* 1999; **83**: 902–910.
- 10 Williamson TH, Keating D. Telemedicine and computers in diabetic retinopathy screening. Commentary. *Br J Ophthalmol* 1998; **82**: 5–7.
- 11 Newsom RSB, Sinthanayothin C, Boyce JF, Casswell AG, Williamson TH. Clinical evaluation of 'local contrast enhancement' for oral fluorescein angiograms. *Eye* 2000; **14**: 318–323.
- 12 Toulson DL, Boyce JF. Image segmentation using a neural network. IEE Colloquium on 3-D Imaging Techniques For Medicine, April 1991.
- 13 Toulson DL, Boyce JF. Segmentation of MR images using neural nets. *Proceedings of the British Machine Vision Conference* 1991: 284–292.
- 14 Toulson DL, Boyce JF. Segmentation of MR images using neural nets. *Image Vis Comput* 1992; **10**: 324–328.
- 15 Gonzales RC, Woods RE. *Digital Image Processing*. Reading: Addison-Wesley Publishing Co., 1993: 229–237, 583–586.
- 16 Gardner GG, Keating D, Williamson TH, Elliot AT. Automatic detection of diabetic retinopathy using an artificial neural network: a screening tool. *Br J Ophthalmol* 1996; **80**: 940–944.
- 17 British Diabetic Association. *Retinal Photography Screening for Diabetic Eye Disease*. London: British Diabetic Association, 1997.
- 18 Javitt JC, Canner JK, Frank RG, Steinwachs DM, Sommer A. Detecting and treating retinopathy in patients with type I diabetes mellitus. A health policy model. *Ophthalmology* 1990; **97**: 483–494.