Computers in Biology and Medicine 53 (2014) 55–64

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Automated diagnosis of Age-related Macular Degeneration using greyscale features from digital fundus images

Muthu Rama Krishnan Mookiah [a,*], U. Rajendra Acharya [a,b], Joel E.W. Koh [a], Vinod Chandran [c], Chua Kuang Chua [a], Jen Hong Tan [a], Choo Min Lim [a], E.Y.K. Ng [d], Kevin Noronha [e], Louis Tong [f,g,h,i], Augustinus Laude [j]

[a] Department of Electronics and Computer Engineering, Ngee Ann Polytechnic, Singapore 599489, Singapore
[b] Department of Biomedical Engineering, Faculty of Engineering, University of Malaya, 50603, Malaysia
[c] School of Electrical Engineering and Computer Science, Queensland University of Technology, Brisbane, QLD 4000, Australia
[d] School of Mechanical and Aerospace Engineering, Nanyang Technological University, Singapore 639798, Singapore
[e] Department of E&C, St. Francis Institute of Technology, Mumbai, 400103, India
[f] Singapore National Eye Center, Singapore 168751, Singapore
[g] Ocular Surface Research Group, Siganpore Eye Research Institute, Singapore 168751, Singapore
[h] Duke-NUS Graduate Medical School, Singapore 169857, Singapore
[i] Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore
[j] National Healthcare Group Eye Institute, Tan Tock Seng Hospital, Singapore 308433, Singapore

ARTICLE INFO

Article history:
Received 14 March 2014
Accepted 20 July 2014

Keywords:
Age-related Macular Degeneration
Entropy
Texture
Higher order spectra
Gabor wavelet
Computer aided diagnosis

ABSTRACT

Age-related Macular Degeneration (AMD) is one of the major causes of vision loss and blindness in ageing population. Currently, there is no cure for AMD, however early detection and subsequent treatment may prevent the severe vision loss or slow the progression of the disease. AMD can be classified into two types: dry and wet AMDs. The people with macular degeneration are mostly affected by dry AMD. Early symptoms of AMD are formation of drusen and yellow pigmentation. These lesions are identified by manual inspection of fundus images by the ophthalmologists. It is a time consuming, tiresome process, and hence an automated diagnosis of AMD screening tool can aid clinicians in their diagnosis significantly. This study proposes an automated dry AMD detection system using various entropies (Shannon, Kapur, Renyi and Yager), Higher Order Spectra (HOS) bispectra features, Fractional Dimension (FD), and Gabor wavelet features extracted from greyscale fundus images. The features are ranked using *t*-test, Kullback–Lieber Divergence (KLD), Chernoff Bound and Bhattacharyya Distance (CBBD), Receiver Operating Characteristics (ROC) curve-based and Wilcoxon ranking methods in order to select optimum features and classified into normal and AMD classes using Naive Bayes (NB), *k*-Nearest Neighbour (*k*-NN), Probabilistic Neural Network (PNN), Decision Tree (DT) and Support Vector Machine (SVM) classifiers. The performance of the proposed system is evaluated using private (Kasturba Medical Hospital, Manipal, India), Automated Retinal Image Analysis (ARIA) and STructured Analysis of the Retina (STARE) datasets. The proposed system yielded the highest average classification accuracies of 90.19%, 95.07% and 95% with 42, 54 and 38 optimal ranked features using SVM classifier for private, ARIA and STARE datasets respectively. This automated AMD detection system can be used for mass fundus image screening and aid clinicians by making better use of their expertise on selected images that require further examination.

1. Introduction

AMD is a chronic irreversible medical condition characterized by drusen or hyper- or hypopigmentations [1]. It is caused due to cell damage in the macula region resulting in central vision loss. AMD is a multi-factorial disease and has various risk factors, viz. age, ocular risk factors namely drusen, retinal pigmentation, choroidal neovascularization and systemic risk factors namely family history, hypertension and smoking [2–5]. AMD is one of the leading sight-threatening diseases among people above 50 years [1,6]. About 20–25 million people are affected globally and it may increase three times in the next 30–40 years with the increase in ageing population [2,7,8]. World Health Organization reported that 8 million people have already been affected with

* Corresponding author. Tel.: +65 64607889.
E-mail address: mkm2@np.edu.sg (M.R.K. Mookiah).

http://dx.doi.org/10.1016/j.compbiomed.2014.07.015
0010-4825/

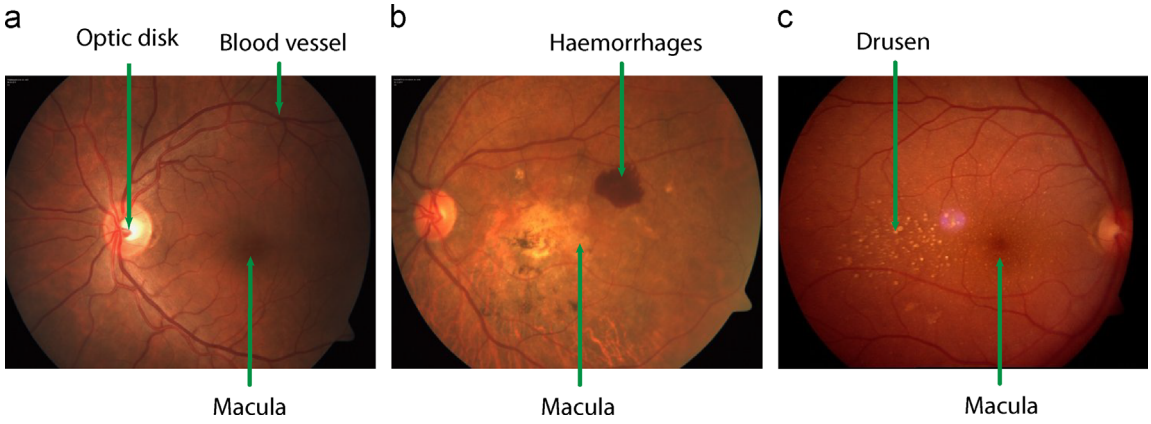

Fig. 1. Typical non-stereo fundus images: (a) normal, (b) wet AMD, and (c) dry AMD.

Table 1
Stages of dry AMD [6,10,2].

Dry AMD stages	Presence of clinical features
Early (see Fig. 2a)	Many small (63 μm in diameter) and few medium (63 μm to 124 μm in diameter) sized drusens (i.e., distinguishable and indistinguishable soft drusens) Retinal pigmentation
Intermediate (see Fig. 2b)	At least one large (124 μm) and many medium sized drusens Lesions present away from the centre of the macula
Advanced (see Fig. 2c)	Drusen in the centre or periphery of the macula Geographic atrophy (area with $\geq$ 175 μm diameter) Neovascular AMD lesions

severe blindness due to AMD [2,7,8]. AMD is mainly classified into two types wet and dry [1,9]. They are briefly explained below:

(i) *Wet macular degeneration* affects the retina due to filling of fluid under the retina [1]. It leads to bleeding (see Fig. 1b) and scarring causing loss of vision. It progresses rapidly and may respond to laser treatment in the early stage [1,10]. Approximately 10% of all people with macular degeneration have the 'wet' type [1,10,11].
(ii) *Dry macular degeneration* is caused by the lack of functioning of visual cells [1]. Initial symptoms of dry AMD are the presence of fatty deposits, called *drusen* (see Fig. 1c), on the retina [12]. There is no treatment for 'dry' type [13]. Most of the people with macular degeneration are affected by the 'dry' type [1,10].

The Wisconsin AMD grading system categorizes drusen based on size and visibility of the boundary, and is adopted in this study. Drusen can be classified as hard or soft. Further, soft drusen is classified as distinguishable or indistinguishable. Retinal pigmentary lesions are grouped into hypo- and hyper-pigmentation [10,2,14]. The presence of clinical features such as drusen, retinal pigmentation and Geographic Atrophy (GA), dry AMD is categorized into three stages, *early*, *intermediate*, and *advance* [6,10,2], which are briefly described in Table 1.

The drusen can be identified by the manual evaluation of retinal fundus images by trained clinicians [6]. Several authors have developed automated drusen segmentation methods, which are the initial step in AMD classification. Automated drusen segmentation methods are briefly described in Table 2.

The important challenge in the above-mentioned methods is the identification of drusen and also differentiating drusen from the background noise and other lesions. Moreover, the variation in the shape and size of drusen varies from image to image causing inaccurate detection of drusen. Hence, traditional image segmentation techniques are not very effective in isolating drusen within the retinal photographs [6].

In this paper we are proposing to classify normal and dry AMD classes *without segmentation* of drusen. The fundus images are preprocessed using adaptive histogram equalization. Further, various non-linear features (FD, HOS entropies, and Gabor wavelet) are extracted from the preprocessed images and ranked using *t*-test, KLD, CBBD, ROC-based and Wilcoxon ranking techniques. Finally, the ranked features are fed to the set of supervised classifiers to identify the best performing classifier. The black diagram of the automated AMD diagnosis system is shown in Fig. 3.

This paper is organized as follows: Image acquisition, preprocessing, feature extraction, ranking and selection are presented in Section 2. Classifiers used for AMD classification are briefly described in Section 3. The results of feature ranking method and various classifiers are explained in Section 4. The obtained results are discussed in Section 5 and a conclusion is provided in Section 6.

2. Materials and methods

2.1. Retinal fundus imaging

Private dataset: The normal and dry AMD fundus images were acquired using TOPCON non-mydriatic retinal camera (TRC-NW200) from Department of Ophthalmology, Kasturba Medical College, Manipal, India. The images were photographed and labelled by the group of ophthalmologist. The hospital ethics committee has approved the image data for research. The five hundred and forty 24-bit Red Green Blue (RGB) colour images (Normal-270 and dry AMD-270) were stored in lossless JPEG format with an image size of 480×364 pixels. The stored AMD images were reviewed by an experienced ophthalmologist and graded into early, intermediate and advance (see Fig. 2) dry AMD images according to Age-Related Eye Disease Study (AREDS) [27] classification.

Public dataset: Two publicly available datasets, viz. ARIA (http://www.eyecharity.com/aria_online) and STARE (http://www.ces.clemson.edu/~ahoover/stare), were also used to test the performance of the proposed AMD detection system. The ARIA dataset consists of 101 normal and 60 AMD images acquired using Carl Zeiss Meditec fundus camera with 50° field of view and a resolution of 768×576 pixels. The STARE dataset consists of 36