Computerized Medical Imaging and Graphics xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Computerized Medical Imaging and Graphics

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

Automated analysis and classification of melanocytic tumor on skin whole slide images

Hongming Xu[a], Cheng Lu[a,b,c], Richard Berendt[d], Naresh Jha[d], Mrinal Mandal[a,*]

[a] Department of Electrical and Computer Engineering, University of Alberta, Edmonton, AB T6G 1H9, Canada
[b] College of Computer Science, Shaanxi Normal University, Xi'an, Shaanxi 710119, China
[c] Department of Biomedical Engineering, Case Western Reserve University, Cleveland, OH 44106, USA
[d] Department of Oncology, Cross Cancer Institute, University of Alberta, Edmonton, AB T6G 1Z2, Canada

ARTICLE INFO

Keywords:
Melanoma
Nuclei segmentation
Biopsy classification
Epidermis and dermis

ABSTRACT

This paper presents a computer-aided technique for automated analysis and classification of melanocytic tumor on skin whole slide biopsy images. The proposed technique consists of four main modules. First, skin epidermis and dermis regions are segmented by a multi-resolution framework. Next, epidermis analysis is performed, where a set of epidermis features reflecting nuclear morphologies and spatial distributions is computed. In parallel with epidermis analysis, dermis analysis is also performed, where dermal cell nuclei are segmented and a set of textural and cytological features are computed. Finally, the skin melanocytic image is classified into different categories such as melanoma, nevus or normal tissue by using a multi-class support vector machine (mSVM) with extracted epidermis and dermis features. Experimental results on 66 skin whole slide images indicate that the proposed technique achieves more than 95% classification accuracy, which suggests that the technique has the potential to be used for assisting pathologists on skin biopsy image analysis and classification.

1. Introduction

Melanoma is a type of malignant skin cancer developing from abnormal growth of melanocytes (pigment cells). Although melanoma is relatively less common and only accounts for about 5% of all skin cancers (Mokhtari et al., 2014), it is the most dangerous form of skin cancer and causes the most skin cancer deaths. The early recognition of melanoma helps to greatly lower the mortality from this cancer (Maglogiannis and Doukas, 2009). However, it is not trivial to identify melanoma in its early phase, mainly due to the similar appearance between melanoma and benign melanocytic lesions (e.g., moles).

Histological examination of skin biopsy slides is usually considered as the gold standard for melanoma diagnosis. Although pathologists can make a judgement by observing the tissue specimen under a microscope or digitized biopsy on a computer, a few problems exist for manual analysis. First, the manual diagnosis is typically subjective and suffers from intra- and inter-observer variability (Petushi et al., 2006). Second, it is very labor-intensive to analyze the biopsy slide due to the large amount of image data involved. To address these problems, computerized systems which can assist pathologists and provide quantitative evaluations are desired.

In the past decade many researchers have attempted to develop computer-aided analysis techniques on whole slide images (WSI). These works are related to head and neck malignancy detection (Mete et al., 2007), neuroblastoma prognosis (Sertel et al., 2009; Kong et al., 2009), cervical intraepithelial neoplasia diagnosis (Wang et al., 2009), prostate cancer detection (Doyle et al., 2012) and brain tumor classification (Barker et al., 2016). Developing automated analysis technique on WSI is a quite challenging problem as it usually involves processing a large volume of image data (tens of gigabytes or even more) with high computational costs. For fast processing on PC platform, most existing WSI analysis techniques (e.g., Sertel et al., 2009; Kong et al., 2009; Doyle et al., 2012) employ a multi-resolution framework that starts analysis of textural patterns from a lower resolution field and then switches to a higher resolution field for analyzing cytological features. The image color statistics, textural patterns, architectural and morphological features of cell nuclei have been widely-used for WSI analysis to diagnose different cancers.

Since most cytological features of skin biopsies are observed from epidermis and dermis–epidermis (DE) junctional areas, a few research works that analyze skin epidermis or DE junctional areas have been proposed. Smolle (2000) proposed a tissue counter analysis (TCA) technique to segment epidermis and dermis layers in skin biopsy images. This technique first divides the image into many non-

* Corresponding author.
E-mail address: mmandal@ualberta.ca (M. Mandal).

https://doi.org/10.1016/j.compmedimag.2018.01.008
Received 27 June 2017; Received in revised form 24 December 2017; Accepted 18 January 2018

overlapping subregions, and then extracts colors and textures in each subregion for statistical analysis and classification. Wiltgen et al. (2003) applied the TCA technique to classify benign nevus and malignant melanoma. Although a good classification accuracy (about 92%) is reported, its performance is sensitive to staining variations as the TCA technique is completely replied on color and texture analysis (Smolle et al., 2002). Miedema et al. (2012) proposed a technique to distinguish melanoma from nevus by using cytological and textural features in skin DE junctional areas. Nielsen et al. (2014) proposed an automated technique that differentiates melanoma and nevus based on quantification of MART1-verified Ki-67 indices in skin epidermis and dermis areas. These techniques only consider a representative region within the WSI. The selection of representative regions requires interactive manual operation. In addition, analysis of representative regions may bring the sampling bias into the diagnostic system.

Recently Lu and Mandal (2015) proposed an automated technique for analysis and diagnosis of melanoma on skin WSI. This technique first segments skin epidermis layer, then computes a set of cytological features from epidermis regions for skin tissue classification. Note that during the real evaluation by pathologists, in addition to epidermis examination, dermis examination is also important because melanoma may invade into skin dermis tissue. Nuclear densities and types in dermis regions often vary from one another among different skin tissues, and hence cytological and textural features of dermis areas are important for automatic melanoma diagnosis. Fig. 1 shows examples of H&E stained skin histological images, where Fig. 1(a)–(c) show normal skin, benign nevus and malignant melanoma, respectively. As observed in Fig. 1, the epidermis presents relatively darker color than the dermis. There is a high density of cell nuclei (keratinocytes and melanocytes) in epidermis of all three skin tissues. In comparison, the dermis has a low density of cell nuclei in normal skin tissue shown in Fig. 1(a), but has a high density of cell nuclei in the nevus and melanoma shown in Fig. 1(b) and (c). In Fig. 1(b) cell nuclei within the dermis are mainly melanocytes which have roughly uniform color and size, while in Fig. 1(c) cell nuclei within the dermis includes both melanocytes (e.g., with irregular nuclear shape and size) and lymphocytes (e.g., small, round and dark nuclei).

In this paper, we propose an automatic technique for analysis and classification of melanocytic tumor on H&E stained skin WSI, which improves the results from the work (Lu and Mandal, 2015). The main contribution of this work includes: (1) a skin WSI analysis framework is proposed for melanocytic tumor classification, (2) both epidermis and dermis features are computed for analysis, which achieves a superior performance for melanoma diagnosis. The organization of this paper is as follows. Section 2 describes the proposed technique, followed by the performance evaluations in Section 3. The conclusion is presented in Section 4.

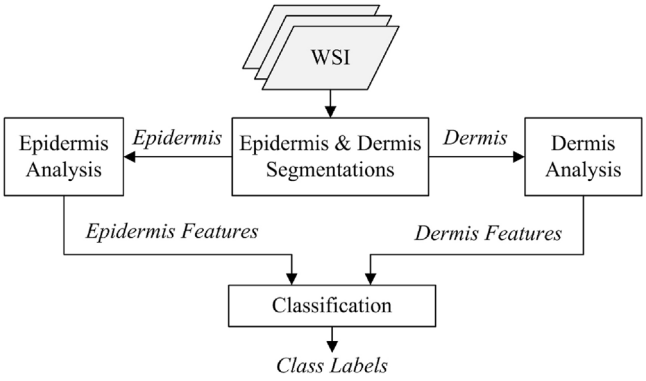

Fig. 2. Schematic of the proposed technique.

2. Proposed technique

The schematic of the proposed technique is shown in Fig. 2. It is observed that the proposed technique consists of four main modules. First epidermis and dermis regions are segmented from skin WSI. Next, epidermis and dermis analysis are performed in a parallel manner. In the epidermis analysis, a set of epidermis features reflecting nuclei morphologies and spatial distributions are computed. In the dermis analysis, a set of textural features and cytological features are computed from dermis regions. Finally, the computed epidermis and dermis features are utilized by a mSVM method that classifies the input skin WSI into different categories. Details of the four modules are presented in the following.

2.1. Epidermis and dermis segmentations

Cytological features within epidermis and DE junctional areas are very critical for melanoma diagnosis. In this module, skin epidermis and dermis are segmented from the WSI such that the subsequent image analysis is focused on these regions. This module includes four main steps: down-sampling, epidermis segmentation, dermis segmentation and image tiles generation, which are explained as follows:

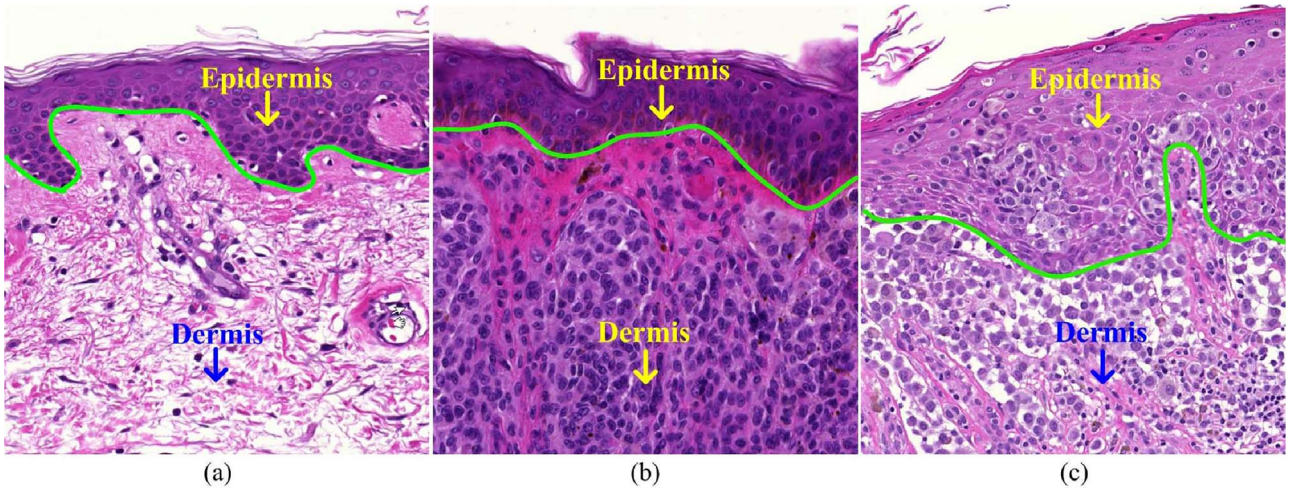

Fig. 1. Examples of H&E stained skin images. (a) Normal skin. (b) Benign nevus. (c) Malignant melanoma. Note that in (a–c) green contours indicate the borders of epidermis and dermis regions. Cell nuclei in both epidermis and dermis regions are observed as blue blobs. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)