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Computer aided measurement of melanoma depth of invasion in microscopic images

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ABSTRACT

This paper presents a novel computer aided technique for measurement of melanoma depth of invasion. Melanoma is the deadliest form of skin cancer with worldwide increasing incidences. For a conclusive diagnosis of melanoma, skin biopsies should be examined under a microscope. Visual inspection of microscopic samples is often subjective, time-consuming, cumbersome and prone to human errors. This fact demonstrates the necessity of developing an automated method which assists pathologists in evaluating histopathological samples more accurately in the busy clinical environment. To the best of our knowledge, this is the first time that a computer-assisted diagnosis algorithm has been applied in measurement of melanoma invasion depth. The proposed method uses a clustering algorithm for granular layer extraction and a pre-trained SVM classifier for detection of malignant melanocytes. The experimental results with average error of 3.9 μm demonstrate that the proposed method is reliable and effective.

1. Introduction

Melanoma is an aggressive form of skin cancer developing in melanocytic system. Pigment-producing cells, called melanocytes predominantly exist in skin, but are also found in other organs, such as the bowel and the eye. Uncontrolled proliferation of these cells leads to melanoma. Melanoma can emerge in any part of the body containing melanocytes. Studies have shown that melanoma is linked to exposure to ultraviolet (UV) radiation and getting severe sunburns (Rigel et al., 2010).

Melanoma is regarded as a rare type of skin cancers. It accounts for roughly 5% of all skin cancers, but it ranks as the deadliest form of skin cancer with an increasing incidence being seen worldwide annually. It may metastasize to other parts of the body via lymphatic system or bloodstream (Daga, 2007).

Early diagnosis of melanoma and grading its evolution is of great significance for treatment and prognosis. The initial diagnosis of melanoma is through clinical examination. Clinical features of melanoma are summarized using the 'ABCD' acronym, standing for Asymmetry, Border irregularity, Color variegation and Diameter. This mnemonic has also been extended through the addition of 'E' for Evolution (Rigel et al., 2010). Although there are many emerging techniques, e.g., epiluminescence dermoscopy, full-body photography and confocal microscopy, the most accurate diagnostic method to confirm or rule out melanoma is histopathological assessment of microscopic samples. Besides, microscopic examination is mandatory to check for probable metastases. There are several indicators used to describe staging of melanoma, namely Breslow's and Clark's indices which both are based on the depth of melanoma invasion. Breslow's index is measured vertically from the top of the stratum granulosum or granular layer of the epidermis downward. Clark's level (replaced by AJCC[1] depth) classifies vertical growth of melanoma (Friedlander, 2008). These methods help physicians determine the kind of treatment and the risk of recurrence after treatment.

Visual assessment of microscopic samples by pathologists is often prone to intra- and inter-observer variance due to fatigue and inexperience. Pathologist must inspect a large number of specimens for any deviation of normal which may be very delicate or rare. A computer based system which indicates subtle signs and suspicious locations to pathologist can reduce workload and probable observational oversights significantly. With recent increases in processing and computing power and improvements in image analysis algorithms, computer aided approaches are applied widely in

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the detection and differential diagnosis of abnormalities in medical images. Computerized image analysis provides more precise diagnostic clues for clinicians to evaluate and interpret histological data. The objective of this paper is to develop an automated scheme, which can help pathologists in correct grading of melanoma by measuring how deeply it has invaded in biopsy images.

The history of Computer Aided Diagnosis (CAD) dates back to the 1980s (Doi, 2007). Over the past three decades, most of the CAD systems have been developed for radiological images and to date, commercial CADs exist for this type of images. However, the automated analysis of histological images is relatively new. Unlike gray scale radiology images, histological images are colored and much larger in size. Histological images can be further categorized into one of two sub-groups: histopathological images and cytological images. While cytological images are characterized by isolated cells, the presence of complicated structures and low contrast between cells and extracellular matrix in histopathological images present a new set of challenges to the image analysis community.

As a continuation of our previous work (Malekian et al., 2013) in the field of developing CADs for histological image analysis, this work is allocated to develop a computer aided method for measurement of melanoma depth of invasion. There are many publications on automated recognition of melanoma based on epiluminescence dermoscopy (Rahman and Bhattacharya, 2010; Dreiseitl et al., 2009; Fabbrocini et al., 2010; Ganster et al., 2001; Celebi et al., 2007; Piatkowska et al., 2011). Ali and Deserno (2012) provided a comparative review on CAD systems based on dermoscopic images. Dhawan et al. (2009) proposed an automated method based on multispectral optical imaging of skin-lesions. There is also published literature covering confocal imaging (Gareau et al., 2010; Kurugol et al., 2011). However, computerized assessment of histological images is still new. He et al. (2012) provided a review on histopathological image analysis. Dhinagar et al. (2011) proposed an automated algorithm for segmentation of main layers of skin tissue (i.e. epidermis, dermis and hypodermis). Babu et al. (2010) presented a method based on Orientation Sensitive Fuzzy C-means for segmentation of dermal–epidermal junction. Lu et al. (2013) proposed an automated algorithm based on radial line scanning for detection of melanocytes. This paper contributes a novel automated method for measurement of melanoma depth of invasion.

The rest of the paper is organized as follows: Section 2 covers the materials and methods of the paper including image acquisition and every step of the proposed method in detail. Results are presented in Section 3. Finally, a conclusion is drawn in Section 4.

2. Materials and methods

The histological samples we used in this work are stained with H&E. Fig. 1 shows the cross-section of a skin tissue sample. As can be seen, hematoxylin stains the nucleus of melanocytes in dark blue whereas eosin stains cytoplasm and other intracellular/extracellular materials white or bright pink. Tumor cells containing melanin pigmentation are seen brown.

The digital microscopic images of tissues were captured using an optical microscope mounted with a Sony CCD (Cyber-shot DSC-H9) camera. 40 images were obtained for analysis from the pathology lab of Al-Zahra Hospital, Isfahan. Senior pathologists determined malignant melanoma in these images.

Fig. 2 demonstrates the overall block diagram of the proposed method.

In order to determine how deep melanoma has spread, the distance from the granular layer to the deepest malignant melanocyte should be measured. To accomplish this, the image is converted to a gray scale version and after some preprocessing epidermal layer

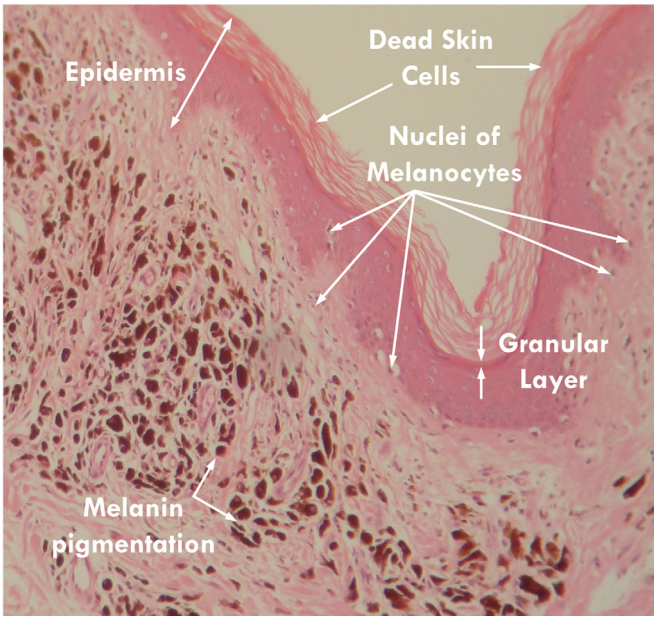

Fig. 1. Representative sample of skin tissue under 10× magnification: brown pigments can clearly be recognized even as melanocytes are rare or unstained. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

is extracted by setting an adaptive threshold. The granular layer is a thin layer of cells on top of the epidermis. In parallel, malignant melanocytes are segmented in the colored image. By merging the results of the two phases, the depth of invasion is computed. Each block is described in more detail in the following sections.

2.1. Segmentation of epidermal layer

As shown in Fig. 1 the images under inspection contain multiple types of tissue constituents. Epidermal layer is extracted from gray scale images by means of an unsupervised clustering algorithm. The major challenge lies in inhomogeneous background. To suppress other unwanted components, a morphological closing filter is applied on gray level images followed by nonlinear histogram equalization.

2.1.1. Morphological filtering

Morphological image processing is a branch of image processing based on shape concept and set theory. The basic idea in morphology is to transform an image with a pre-defined shape, called the structuring element (also known as a kernel). The two fundamental morphological operators are dilation and erosion. Other operations could be extracted from these two basic ones.

The dilation of a binary image by a structuring element generally enlarges the objects in the image such that the intersection of the input image with the translated kernel is not empty. Contrary, erosion is the operation of shrinking so that all the pixels in the translated kernel are a subset of the input image. Closing is

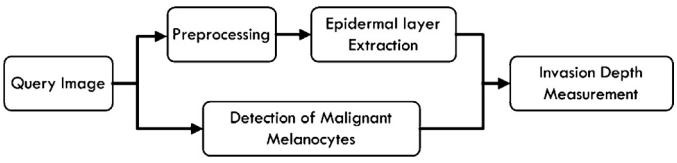

Fig. 2. Block diagram of the proposed computerized method for measurement of melanoma invasion depth.