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Detection of melanocytes in skin histopathological images using radial line scanning

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ABSTRACT

In the diagnosis of skin melanoma by analyzing histopathological images, the detection of the melanocytes in the epidermis area is an important step. However, the detection of the melanocytes from the epidermis area is difficult because other keratinocytes that are very similar to the melanocytes are also present. This paper proposes a novel computer-aided technique for detection of the melanocytes in the epidermis area of skin histopathological images. An adaptive threshold technique is first applied to segment all the keratinocytes in the image. In order to distinguish the melanocytes from other keratinocytes, a novel technique based on radial line scanning is proposed to estimate the halo region of the melanocytes. Based on the estimated halo region of all the nuclei, an area ratio of estimated halo region and the nuclei is used to detect the melanocytes from all the keratinocytes. Experimental results on 40 different histopathological images of skin tissue containing 341 melanocytes show that the proposed technique provides a superior performance.

1. Introduction

Skin cancer is the most frequent and malignant types of cancer [14] and melanoma is the most aggressive type of skin cancer. According to a recent article, approximately 70,000 people are diagnosed with melanoma skin cancer, and about 9000 die from it in the United States every year [22]. The early detection of malignant melanoma will help to lower the mortality from this cancer. Approaches to melanoma diagnosis have dynamically evolved during the last 25 years [18]. Although there are many new emerging techniques, e.g., confocal microscopy [16], which could provide satisfactory performance, pathological examination remains the gold standard for diagnosis as the histopathology slides provide a cellular level view of the disease [10].

Traditionally, the histopathology slides are examined under a microscope by pathologists. The diagnosis decisions are then made based on their personal experience. However, this judgement is subjective and often leads to intra-observer and inter-observer variability [7,19,8,1,4]. For example, it has been reported that in the diagnosing of follicular variant of papillary carcinoma (FVPC), the inter-observer agreement on benign and malignant diagnoses is only 27% from 6 experts on 15 cases, and the intra-observer agreement range from 17% to 100% [4]. Ruijter et al. [19] stated that at least 17% of all the grading errors result from the misinterpretation of the pathologists. To address this problem, automated computational tools are needed which can provide reliable and reproducible objective results.

In melanoma diagnosis, the segmentation and detection of the melanocytes in the epidermis area is an important step before the diagnosis is made. If the melanocytes can be found correctly, architectural and cellular features (e.g. size, distribution, location) can then be used to grade or determine the malignancy of the melanotic skin tissue.

In the epidermis area of skin, a normal melanocyte is typically a cell with a dark nuclei, lying singly in the basal of epidermis. However, in the melanoma or nevus, the melanocytes are abnormally growing, and can be distributed in the middle layer of epidermis. The digitized histopathological image we used in this work is stained with haematoxylin and eosin (H&E). Three examples of the skin epidermis image are shown in Fig. 1(a)–(c). The cell nuclei are observed as dark blue whereas the intra-cellular material and cytoplasm are observed as bright pink. Note that the bright seed points indicate the location of melanocytes whereas other nuclei are the other keratinocytes. It is observed that the differences between melanocytes and other keratinocytes are the surrounding region. In the case of melanocyte, it appears to lie in a brighter halo-like region and retracted from other cells, due to the shrinkage of cytoplasm [23]. One close up example of the melanocyte is shown in Fig. 1(d), where the outer dotted contour

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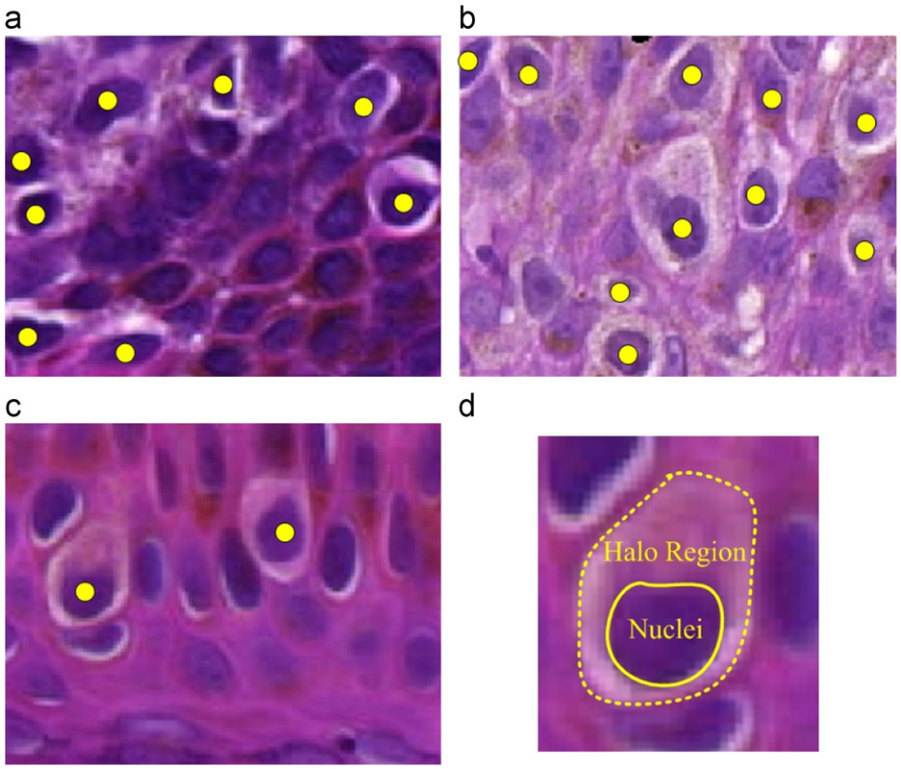

Fig. 1. Melanocytes in epidermis area from different skin tissues. Inter- and intra-image variations are observed in terms of the color. These images are sampled from the skin digitized slide under 30 × magnification. In (a)–(c), the bright seed points indicate the location of melanocytes whereas other nuclei are keratinocytes. (d) A close up image of a melanocyte. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of this article.)

represents the halo region and the inner solid contour represents the nuclei. In contrast, the other keratinocytes are closely contact with the cytoplasm and it has no or little brighter area. The brighter halo-like region of the melanocyte is an important pattern for differentiation of the melanocytes and other keratinocytes. In this work, we refer this pattern as "MPattern" and the bright region around the melanocytes as *halo regions*.

Several works have been conducted on the segmentation or detection of various biological components in the histopathological image using image processing techniques such as thresholding [6,17,12] and watershed [3]. These techniques typically fail when considerable intensity variations are present in the images. By incorporating the image color, texture and shape information, Naik et al. [15] proposed to segment the nuclei using the Bayesian classifier. Sertel et al. [20] computed the probability map of karyorrhexis cells based on the estimated likelihood function, and the cell nuclei are then segmented using thresholding. Although these techniques have been reported to provide good performance, the performance is sensitive to the training samples.

In the melanocytes detection problem, the main difficulty is how to differentiate the melanocytes and other keratinocytes in the skin epidermis area. Similar problem has been addressed by Basavanhally et al. [2] in breast cancer diagnosis where the lymphocyte nuclei are differentiated from the cancer cell nuclei in H&E stained histopathological images. In their work, the basic assumption to differentiate two kinds of cells is based on the domain knowledge regarding the nuclei size, intensity of the nuclei and spatial proximity. However, in skin histopathological images, the size of melanocytes are very similar to that of other keratinocytes. In addition, the intensity value of the melanocytes and other keratinocytes are very close to each other. Therefore, the domain knowledge used in breast cancer [2] does not work well in the case of melanocytes detection.

There is another closely related work in the literature where the keratinocytes nuclei are segmented in the skin epidermis area [9]. In this work, a threshold is decided based on the assumption that cell nuclei covers approximately the darkest 20% pixels in the image. The pixels whose values are less than the threshold are labeled as nuclei regions. Morphological operations are then used to do the refinement. However, this global threshold based technique only works under the assumption that there are no intensity variations in the image and usually generate the under-segmentation results (many of the nuclei are grouped together). Also, there is no attempt to differentiate the melanocytes and other keratinocytes.

Template matching technique is a popular technique in computer vision for pattern detection. Naik et al. [15] have used four binary elliptical templates with different major and minor axes to detect the nuclei in breast cancer histopathological images. It is observed in Fig. 1 that the melanocytes typically have low intensity value while its spatial surrounding space presents a brighter intensity value. It may be possible to detect the melanocytes using a template matching technique with templates that have similar appearance of the melanocyte. However, several difficulties need to be addressed. First, the size of the template is hard to decide due to the size variations of the melanocytes even under the same magnification level. In the case of cancer skin, the melanocytes are abnormal and larger than that in the case of normal skin or nevus skin. Second, the intensity level of the template is hard to determine. Therefore, it is difficult to decide a 'good' template to match the melanocyte patterns.

In this paper, we propose a novel technique to detect the melanocytes in the skin epidermis area. To our best knowledge, this is the first automated technique for the detection of the melanocytes in histopathological image of skin tissue. This technique operates on reliable quantitative measures and provides