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# Differential diagnosis of squamous cell carcinoma in situ using skin histopathological images

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ABSTRACT

Differential diagnosis of squamous cell carcinoma in situ is of great importance for prognosis and decision making in the disease treatment procedure. Currently, differential diagnosis is done by pathologists based on examination of the histopathological slides under the microscope, which is time consuming and prone to inter and intra observer variability. In this paper, we have proposed an automated method for differential diagnosis of SCC in situ from actinic keratosis, which is known to be a precursor of squamous cell carcinoma. The process begins with epidermis segmentation and cornified layer removal. Then, epidermis axis is specified using the paths in its skeleton and the granular layer is removed via connected components analysis. Finally, diagnosis is done based on the classification result of intensity profiles extracted from lines perpendicular to the epidermis axis. The results of the study are in agreement with the gold standards provided by expert pathologists.



## 1. Introduction

Cutaneous squamous cell carcinoma (SCC) is the second most common form of skin cancer, constituting about 20% of all reported cases of non-melanoma skin malignancies [1,2]. It arises from uncontrolled growth of squamous cells in the upper layer of the skin tissue and has the potential to metastasize to other organs of the body if left untreated. Squamous cell carcinoma in situ, also called intra-epidermal SCC or Bowen disease, is the first stage of SCC. “In situ” means that the malignant cells are still only in the epidermis and have not invaded deeper into the dermis [3].

Differential diagnosis is the procedure of distinguishing a particular disease from others that present similar clinical signs, e.g. differentiating between prostate cancer and benign prostatic hyperplasia. In the case of SCC in situ, there are number of skin lesions that should be considered in differential diagnosis, among which, actinic keratosis and basal cell carcinoma (BCC) are more remarkable [3].

Differential diagnosis of SCC in situ versus actinic keratosis is not a trivial task as both share similar clinical and histological features. Currently, differential diagnosis is done by pathologists based on examination of the histopathological slides under the microscope, which is laborious, time consuming and prone to inter and intra observer variability. Moreover, there are relatively few expert pathologists against the large number of tissue samples to be investigated. So, automated systems for analyzing the histopathological slides are desirable.

Actinic keratosis is commonly believed to be a precursor of squamous cell carcinoma in situ and is referred to as incipient SCC by some authors [4], because it can progress to invasive squamous cell carcinoma if left untreated. Hence, in this work, the problem of distinguishing SCC in situ from actinic keratosis is addressed.

Skin is composed of three primary layers: epidermis, dermis and hypodermis (subcutaneous adipose layer). Epidermis is divided into three layers: Malpighian (basal and squamous) layer, granular layer and cornified layer. Fig. 1a shows a histopathological image of normal skin in which the two main layers, epidermis and dermis are indicated. Cells existing in basal and squamous layer are called keratinocyte.

In pathology, SCC in situ is recognized by the presence of dysplastic keratinocytes which cover the full-thickness of epidermis and in advanced stages, invade the dermis [3]. Dysplastic keratinocytes are immature cells with a relatively high nucleus to cytoplasm (N:C) ratio, the ratio which indicates the maturity of a cell [5]. As a cell matures, this ratio generally decreases. Unlike healthy cells, cancerous cells reproduce very quickly and do not have a chance to mature. Other pathological cues to rule out SCC in situ are cells polymorphism, hyperkeratosis (thickened cornified layer), parakeratosis (presence of keratinocytes nucleus in cornified layer) and increase in epidermis layer thickness. Actinic keratosis is also characterized by the above mentioned cues specially dysplastic keratinocytes in epidermis layer, but it differs from SCC in situ in the way that abnormal cells present mainly in *lower third* of the epidermis [3,6].

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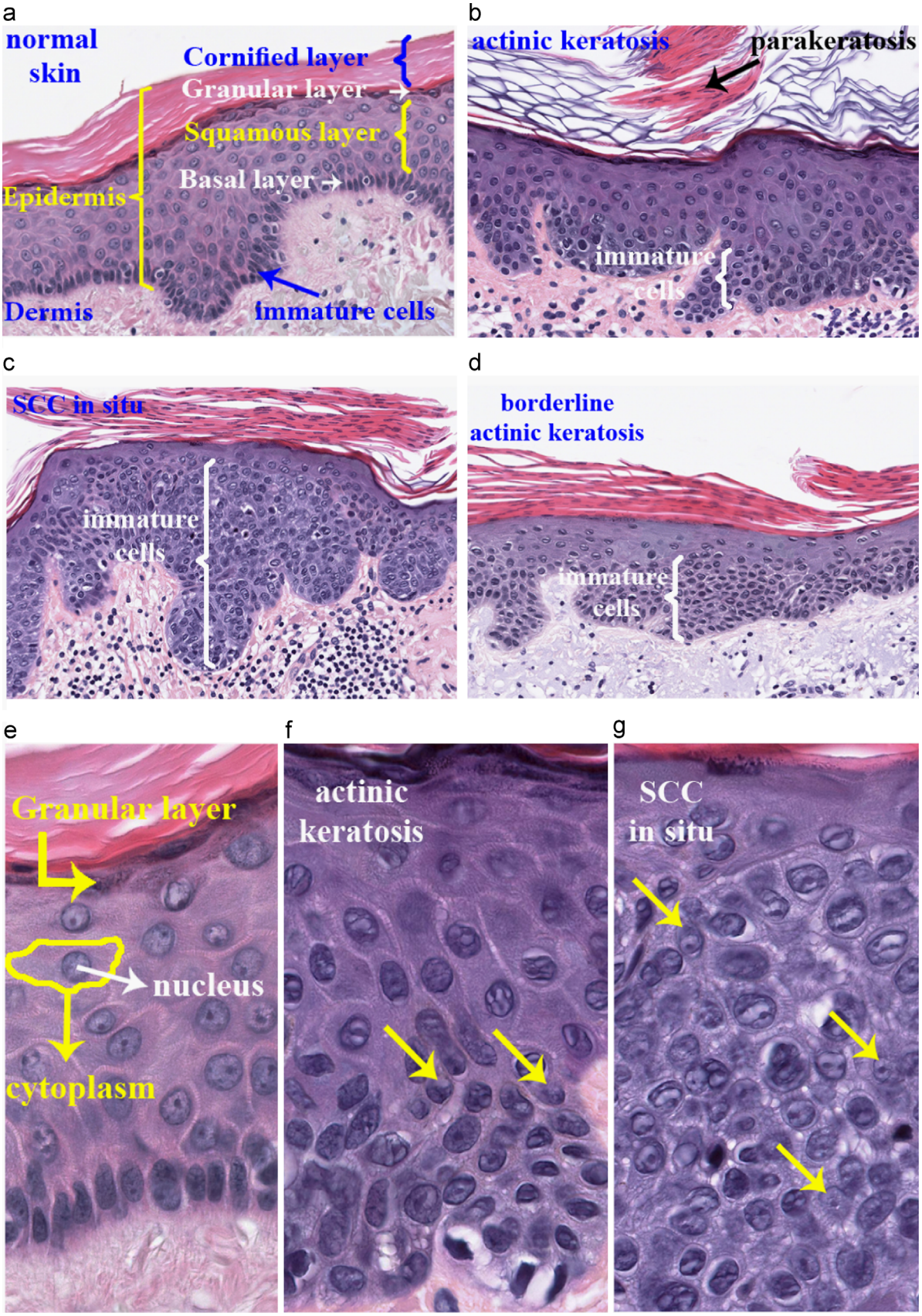


**Fig. 1.** Skin histopathological images of (a) normal case, (b) actinic keratosis, (c) SCC in situ, and (d) borderline case. White brackets in (b)–(d) indicate the areas covered by atypical keratinocytes. (e)–(g) Magnified views of vertical strips cropped from epidermis area in (a)–(c). Yellow arrows in (f) and (g) show cluttered cells with poorly defined membranes. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)