UC BIC Conference 2022

Deep learning-based non-invasive skin virtual histology using reflectance confocal microscopy

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300-word abstract

Introduction:

An invasive biopsy followed by histological staining is the gold standard for traditional pathological identification of skin cancers, which requires a long processing time and often results in undesired biopsies and scarring. Reflectance confocal microscopy (RCM) can provide biopsy-free *in vivo* images of skin structure with a cellular-level resolution for skin disease evaluation; however, the RCM images are grayscale, miss nuclear features and have a low correlation with pathology, which requires specialized training for interpretation. Here, we report a deep learning-

based method for performing non-invasive virtual skin histology using *in vivo*, label-free RCM images.

Approach:

We trained a convolutional neural network (CNN) using *ex vivo* RCM images of excised unstained tissue as inputs and RCM images of the same tissue stained with acetic acid as ground truth so that *in vivo* RCM images of unstained skin can be rapidly transformed into virtually acetic acid-stained tissue images with nuclear contrast revealed. Following that, a second CNN is trained to transform these acetic acid virtual staining results into hematoxylin and eosin-like images.

Results:

We demonstrated that this framework is applicable to different conditions, including normal skin, basal cell carcinoma, and melanocytic nevi with pigmented melanocytes, as well as images of different skin layers, including epidermis, dermal-epidermal junction, and superficial dermis. We validated the success of our *ex vivo* acetic acid virtual staining results by quantifying the nuclear prediction performance and the nuclear morphological characteristics, which presented a good match with those calculated based on the actual acetic acid-stained ground truth images. Our *in vivo* virtual staining results were also compared to histochemically stained counterparts excised from the same tissue, showing histological features similar to traditional H&E histology. This method of virtual skin histology may be transformative for rapid diagnosis of malignant skin neoplasms and reduce invasive skin biopsies.