Biopsy free virtual histology to discriminate benign from malignant squamous neoplasms

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Abstract:

Reflectance confocal microscopy (RCM) is a noninvasive optical imaging modality that allows for cellular-level resolution, in vivo images of skin without performing a traditional skin biopsy. RCM image interpretation currently requires specialized training to interpret the grayscale output images that are difficult to correlate with tissue pathology. Here, we use a deep learning-based framework that uses a convolutional neural network to transform grayscale output images into virtually-stained hematoxylin and eosin (H&E)-like images allowing for the visualization of various skin layers, including the epidermis, dermal-epidermal junction, and superficial dermis layers. To train the deep-learning framework, a stack of a minimum of 7 time-lapsed, successive RCM images of excised tissue were obtained from epidermis to dermis 1.52 microns apart to a depth of 60.96 microns using the Vivascope 3000. The tissue was embedded in agarose tissue and a curette was used to create a tunnel through which drops of 50% acetic acid was used to stain cell nuclei. These acetic acid-stained images were used as “ground truth” to train a deep convolutional neural network using a conditional generative adversarial network (GAN)-based machine learning algorithm to digitally convert the images into GAN-based H&E-stained digital images. We used the already trained machine learning algorithm and retrained the algorithm with new samples to include squamous neoplasms. Through further training and refinement of the algorithm, high-resolution, histological quality images can be obtained to aid in earlier diagnosis and treatment of cutaneous neoplasms. The overall goal of obtaining biopsy-free virtual histology images with this technology can be used to provide real-time outputs of virtually-stained H&E skin lesions, thus decreasing the need for invasive diagnostic procedures and enabling greater uptake of the technology by the medical community.

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