

Applying virtual histology to reflectance confocal microscopy to distinguish malignant from benign cutaneous squamous neoplasms

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Reflectance confocal microscopy (RCM) is a noninvasive optical imaging technique that uses a laser to capture cellular-level resolution images based on differing refractive indices of tissue elements. RCM image interpretation is challenging and requires training to interpret and correlate the grayscale output images that lack nuclear features with tissue pathology. Here, we utilize a deep learning-based framework that uses a convolutional neural network to transform grayscale images into virtually-stained hematoxylin and eosin (H&E)-like images enabling the visualization of various skin layers. To train the deep-learning framework, a series of a minimum of 7 time-lapsed, successive “stacks” of RCM images of excised tissue, spaced 1.52μ apart to a depth of 60.96μ were obtained using the Vivascope 1500. The tissue samples were stained with a 50% acetic acid solution to enhance cell nuclei. These images served as the “ground truth” to train a deep convolutional neural network with a conditional generative adversarial network (GAN)-based machine learning algorithm to digitally convert the images into GAN-based H&E-stained digital images. The machine learning algorithm was initially trained and subsequently retrained with new samples, specifically focusing on squamous neoplasms. The trained algorithm was applied to skin lesions that had a clinical differential diagnosis of squamous neoplasms including squamous cell carcinoma, actinic keratosis, seborrheic keratosis, and basal cell carcinoma. Through continuous training and refinement, the algorithm was able to produce high-resolution, histological quality images of different squamous neoplasms. This algorithm may be used in the future to facilitate earlier diagnosis of cutaneous neoplasms and enable greater uptake of noninvasive imaging technology within the medical community.