

Combining portable reflectance confocal microscopy with machine learning for rapid “virtual” histology of residual tumor after biopsy

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Defining the presence of residual tumor and margins may enhance tissue sparing in dermatologic surgery, but no device serves this role. Reflectance Confocal Microscopy (RCM) provides non-invasive cellular level resolution of the skin, but the FDA-approved RCM device is rigid and requires a tissue cap making tissue mapping difficult. We previously applied “virtual histology”, a deep-learning algorithm to RCM images to generate biopsy-free histology, however, whether virtual histology can be applied to images obtained with a portable, handheld RCM device to scan for residual tumor and margins is unknown. We hypothesize that combining a handheld device with virtual histology could provide accurate tumor assessment and these virtual histology images would correlate with traditional histology. The study was conducted as a prospective, consecutive non-randomized trial at a VA Medical Center dermatologic surgery clinic. Patients over 18 years old with confirmed BCC, SCC, or SCCis were included. Successive *in-vivo* confocal images from the epidermis and dermis were obtained with the handheld device and processed through a conditional generative adversarial network-based algorithm to create H&E pseudo-stained virtual histology. The algorithm produced similar virtual histology of *in-vivo* RCM images from the handheld and standard device, demonstrating successful application to the handheld device. Virtual histology applied to handheld RCM images capturing residual tumor, precancerous lesions (actinic keratosis) and scar tissue correlated with Mohs frozen section histology from excised tissue. The combination of machine-learning based virtual histology with handheld RCM images may provide histology-quality data in real time for tumor evaluation to assist the surgeon, improving clinical efficiency by decreasing unnecessary surgeries/layers and cosmesis through better margin assessment.