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Fluorescence lifetime imaging and reflectance confocal microscopy for multiscale imaging of oral precancer.

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ABSTRACT

Optical imaging techniques using a variety of contrast mechanisms are under evaluation for early detection of epithelial precancer; however, tradeoffs in field of view (FOV) and resolution may limit their application. Therefore, we present a multiscale multimodal optical imaging system combining macroscopic biochemical imaging of fluorescence lifetime imaging (FLIM) with subcellular morphologic imaging of reflectance confocal microscopy (RCM). The FLIM module images a $16 \times 16 \text{ mm}^2$ tissue area with $62.5 \text{ }\mu\text{m}$ lateral and 320 ps temporal resolution to guide cellular imaging of suspicious regions. Subsequently, coregistered RCM images are acquired at 7 Hz with $400 \text{ }\mu\text{m}$ diameter FOV, $<1 \text{ }\mu\text{m}$ lateral and $3.5 \text{ }\mu\text{m}$ axial resolution. FLIM-RCM imaging was performed on a tissue phantom, normal porcine buccal mucosa, and a hamster cheek pouch model of oral carcinogenesis. While FLIM is sensitive to biochemical and macroscopic architectural changes in tissue, RCM provides images of cell nuclear morphology, all key indicators of precancer progression.