OBJECTIVE TISSUE DIAGNOSIS USING LABEL-FREE MULTIMODAL NON-LINEAR IMAGING AND TEXTURE ANALYSIS

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Rapid quantitative analysis of tissue specimens, either biopsies or resected specimens, is highly desirable for objective diagnosis and intraoperative histopathological analysis in diseases such as cancer. Staining-based histopathology is the gold standard for diagnosing cancer in tissue and relies on experienced pathologists to assess subtle architectural features of stained biological structures at the subcellular, cellular, and tissue levels. It is a subjective practice done remote from the patient and using processed/stained tissue that takes over a few hours to days. Thus, there is a significant need for a more quantitative and rapid imaging-based approach to give pathologists more powerful tools for disease diagnosis.

In this work we demonstrate that the multimodal combination of second harmonic generation (SHG) with multi-colour coherent anti-Stokes Raman scattering (CARS) provides high quality imaging of tissue sections from head & neck squamous cell cancer (HNSCC) patients. With these techniques more detailed features can be visually identified by monitoring collagen, lipids, proteins and carbohydrates compared to conventional H&E stained images. Further, to aid objective diagnosis we have developed a segmentation technique taking into account, in addition to spectral intensities, texture parameters derived from the label-free images which take into account changes in the neighbourhood of different pixels, or 'textels', at different spatial dimensions. This concept has been used to develop a first-order texture characterization tool called Spatial Kernel-based Augmentation (SKA) algorithm. Using SKA combined with multimodal CARS/SHG imaging we are not only able to segment images into epithelium and stroma but also identify normal, dysplastic and cancerous tissue with high specificity and sensitivity using discriminant analysis. Our work paves the way for automated image analysis and objective diagnosis with label-free non-linear imaging techniques for translation to aid clinicians in intra-operative histopathology.

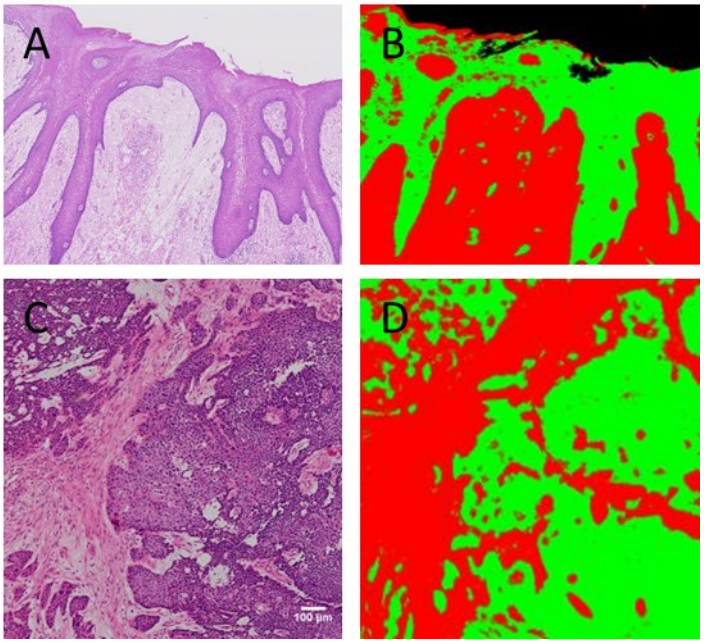

Figure 1. Stained images (A, C) and corresponding segmented images (B, D) obtained using texture analysis of multimodal CARS/SHG images identifying the epithelial (green) and the stromal (red) regions in dysplastic (A, B) and cancer tissue (C, D), respectively.