ABSTRACT

head and neck cancers (HNCs) are rare cancers of mainly *squamous cell carcinoma* (SCC) that do not show symptoms typically associated with cancer in the early stages of development. The main causes are alcohol and tobacco consumption with *human papillomavirus* (HPV) also becoming an increasingly common cause. While treatment is uncomplicated in the early stages, mortality significantly increases if patients do not seek medical attention before the cancer has developed into the later stages. Treatment typically involves surgery and chemoradiotherapy, where the former carries the risk of damaging the delicate organs in the head and neck region. The interface between healthy tissue and tumor is subtle and gradual, which means that surgeons are often dependent on *intra-operative consultations* (IOCs) during operation to determine whether enough tissue has been resected. This process involves transferring (a part of) the resected tissue to the Department of Pathology for macroscopic inspection, flash freezing, microsectioning and microscopic assessment before a response can be returned to the surgeon waiting in the operating theater. Reducing this lag time would result in cost reductions and potentially increased patient throughput as well as the workload at the Department of Pathology.

In this thesis the applicability of a *deep neural network* (DNN) as an automated diagnosing tool was investigated. The hypothesis being that non-invasive imaging modalities, specifically *coherent anti-Stokes Raman scattering* (CARS), *second-harmonic generation* (SHG), and *two-photon excited fluorescence* (TPEF) microscopy, could provide adequate information about a label-free sample for a DNN to learn to recognize different tissue types if presented with a database of such images.

The study in this project shows that the combination of CARS, SHG, and TPEF deliver enough information to positively identify several important features of both healthy, dysplasic, and cancerous tissue. Furthermore, it also showed that a *fully convolutional neural network* (FCNN) can be trained from a relatively small image database and achieve an impressive accuracy. Several hyper parameters were evaluated and we found that the highest performance was achieved with a combination of the novel Swish activation function, batch normalization, the region-based Tversky loss function and a host of input data augmentation algorithms including, but not limited to, random pixel deletion (dropout), rotation and elastic deformation.

The results of this study shows that multi-modal imaging in combination with deep learning-based analysis in the future can help reduce the pathologists workload during IOCs and that more data is needed to improve the performance.