

In Vivo Raman Spectroscopy During Routine Head and Neck Cancer Surgery

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Abstract

Head and neck cancer is among the most prevalent malignancies worldwide, and surgical resection is a major treatment modality. In head and neck squamous cell carcinoma (HNSCC), outcome depends on complete tumor removal while preserving critical function and aesthetics, but intraoperative biopsies with histological assessment remain time-consuming and subjective for real-time decision-making. We established a complete clinical workflow for *in vivo* Raman spectroscopy during head and neck cancer surgery and evaluated its feasibility, safety, and data quality under real operating room conditions. The workflow was implemented as part of a prospective feasibility trial (DRKS00028114) using the Raman InvaScope system and was designed to meet practical intraoperative constraints while complying with investigational medical device requirements.

Intraoperative Raman spectroscopy was performed in 25 patients with HNSCC and 10 patients with inflammation as a clinical control group. Raman measurements were acquired directly from tumor sites, tumor margins, and healthy tissue, with 8–15 spectra per site across heterogeneous anatomical subsites including the oral cavity, oropharynx, larynx, and hypopharynx. Tissue samples were collected from the same locations where Raman measurements were obtained. Histopathological examination of these

samples served as the reference standard for defining the ground truth label of each measured site. A standardized preprocessing pipeline was applied.

Workflow efficiency was quantified using a learning-curve analysis of total acquisition time per patient. Early implementation required >30 minutes per case, which decreased to <5 minutes after the first 15 patients, reaching approximately 2 minutes per patient in later routine intraoperative use. Spectral analysis demonstrated consistent differences between tumor and healthy tissue, with discriminative features observable across both fingerprint and high-wavenumber spectral regions. These spectral differences were consistent with previously reported Raman characteristics of tumor and healthy head and neck tissues, supporting the reliability of the workflow.

We were able to demonstrate that intraoperative *in vivo* Raman spectroscopy can be implemented as a standardized, time-efficient, and safe workflow in head and neck oncologic surgery while generating consistent, interpretable datasets suitable for subsequent development and validation of real-time Raman-based tissue classification.

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