Intraoperative Surgical Decision Making based on Real-Time Biophotonics

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Abstract

Achieving tumor-free surgical margins remains a major challenge in head and neck squamous cell carcinoma (HNSCC) surgery. Conventional frozen section analysis is limited by sampling errors, processing time, and interobserver variability. We believe that combining fast horizontal and precise vertical biophotonic methods can improve intraoperative delineation of tumor boundaries. Our work focuses on marker-free techniques, including nonlinear multimodal imaging, Raman spectroscopy, and hyperspectral imaging (HSI).

For nonlinear multimodal imaging, a rigid endomicroscope was developed and evaluated in a preclinical cohort of 15 patients. Using deep learning–based semantic segmentation to analyze multimodal data, this study achieved a diagnostic sensitivity of 88% and a specificity of 96% for HNSCC detection, demonstrating strong potential for intraoperative application.

In the field of Raman spectroscopy, a clinical workflow has already been established using a fiber-optic Raman probe. In a prospective feasibility trial (DRKS00028114), Raman measurements were performed in 52 patients with HNSCC and control conditions. Spectra were acquired from tumor tissue, resection margins, and healthy mucosa and correlated offline with postoperative histopathology. Integration into the surgical workflow proved feasible and safe, with measurement times reduced to under five minutes after a brief training phase. Spectral analysis using a combination of principal component analysis–linear discriminant analysis (PCA-LDA) and deep learning enabled reliable discrimination between malignant and non-malignant tissue.

For hyperspectral imaging, an ongoing prospective in vivo study (DRKS00033009) uses an endoscopic HSI device to image HNSCC lesions prior to resection. Images are processed through an automated pipeline and validated against annotations from an independent expert surgeon; first results will be presented at the congress. In parallel, HSI combined with deep learning and three-dimensional (3D) tumor modeling is applied to intraoperative biopsies typically used for frozen sections. Volumetric histology models are precisely co-registered with corresponding HSI data, enabling voxel-wise projection of tumor segmentation maps. For six freshly resected HNSCC specimens, deep learning achieved an overall tumor classification

accuracy of 0.98 and a recall of 0.93. The long-term goal is a real-time, ex vivo, HSI-based 3D assessment of bulky specimens to support margin evaluation.

Together, these results demonstrate the feasibility and diagnostic potential of combined intraoperative biophotonic approaches for tumor margin assessment in HNSCC, laying the groundwork for future large-scale validation and clinical translation.

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