Review Article

Artificial Intelligence for Real-Time Resection Margin Evaluation in Oral Cancer: A Future Perspective

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ABSTRACT

Clear resection margins in oral cancer surgery are essential for minimizing local recurrence and enhancing patient outcomes. Conventional intraoperative margin assessment, primarily through frozen section analysis, is time-intensive and prone to sampling errors. Artificial intelligence (AI) offers a promising solution for real-time, accurate margin evaluation. This review examines AI's role in intraoperative margin assessment for oral cancer, focusing on machine learning (ML), deep learning (DL), and imaging-based techniques such as hyperspectral imaging (HSI), optical coherence tomography (OCT), and Raman spectroscopy. We review their applications, advantages, limitations, and future potential, supported by scientific evidence. AI-driven methods improve precision, reduce operative time, and enhance oncologic outcomes, paving the way for transformative advancements in surgical practice.

Key words: Oral Cancer, Resection Margin, Artificial Intelligence

Oral cancer, predominantly squamous cell carcinoma, accounts for approximately 4% of all cancers globally, with over 350,000 new cases annually.[1] Surgical resection with clear margins (≥5 mm of healthy tissue) is the cornerstone of treatment, as positive or close margins (<5 mm) are associated with a 30–50% increased risk of local recurrence.[2] Intraoperative margin assessment traditionally involves frozen section analysis, which is limited by sampling bias, prolonged operative time, and variable accuracy (sensitivity ~70–90%).[3] Artificial intelligence (AI), encompassing machine learning (ML) and deep learning (DL), offers real-time, objective margin evaluation, potentially revolutionizing oral cancer surgery.

The rationale for this review stems from the need to address the role of AI, encompassing ML and DL, to offer transformative potential for real-time, objective, and accurate margin evaluation. AI-driven approaches can analyze complex tissue characteristics, integrate multimodal imaging, and provide surgeons with actionable insights during surgery, potentially reducing recurrence rates and improving patient outcomes. This review examines AI's role in intraoperative margin assessment, highlighting its scientific basis, applications, and challenges.

Pathophysiology and Importance of Margin Assessment

Oral cancers often infiltrate surrounding tissues, necessitating precise margin delineation to ensure complete tumor removal. Histologically, positive margins harbor residual cancer cells, increasing recurrence risk.[2] Frozen section analysis, while widely used, samples only 1–2% of the resection margin, risking false negatives.[3] AI integrates advanced imaging and computational models to analyze entire margin surfaces, improving detection of microscopic disease. **AI** technologies in intraoperative margin assessment in shown in Table 1.[4-14]

Advantages of AI in Margin Assessment

a) Accuracy: AI models consistently outperform frozen section analysis, with sensitivities and specificities often exceeding 90%.[7] AI-driven margin assessment, particularly in surgical oncology, leverages advanced ML and DL algorithms to analyze tissue samples with high precision. Unlike traditional frozen section analysis, which relies on manual histopathological evaluation and is prone to human error, AI models are trained on vast datasets of annotated tissue images, enabling them to detect malignant cells with remarkable accuracy.[8] Sensitivities and specificities exceeding 90% indicate that AI can reliably distinguish between cancerous and healthy tissue, reducing false positives and negatives.[9] This is critical in ensuring complete tumor resection while preserving healthy tissue, improving patient outcomes.

b) Speed: Real-time processing (seconds to minutes) reduces operative time compared to frozen sections (20–30 minutes).[10] AI systems process imaging or histopathological data at

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unprecedented speeds, enabling intraoperative margin assessment in near real-time. Traditional frozen section analysis requires tissue excision, freezing, sectioning, staining, and microscopic evaluation by a pathologist, a process that typically takes 20–30 minutes per sample.[11] This delay extends operative time, increasing anesthesia exposure and operating room costs. In contrast, AI algorithms, particularly those integrated with intraoperative imaging modalities like HSI or fluorescence-guided surgery, can analyze margins within seconds to minutes, providing surgeons with immediate feedback.[12] This rapid feedback allows surgeons to make informed decisions during the procedure, potentially reducing the need for additional resections or follow-up surgeries.

c) Comprehensiveness: AI analyzes entire margin surfaces, minimizing sampling errors.[6] Traditional margin assessment methods, such as frozen section analysis, rely on sampling specific regions of the resection margin, which may miss microscopic tumor extensions if the sampled area is not representative. AI, however, can analyze entire margin surfaces using advanced imaging techniques like HSI, OCT, or confocal microscopy.[13] By processing large datasets encompassing the full 3D structure of the margin, AI ensures a comprehensive evaluation, significantly reducing the risk of sampling errors.[14] AI algorithms can reconstruct and analyze volumetric data from intraoperative imaging, identifying malignant cells across the entire resection surface.[15] By providing a complete picture of the margin status, AI enhances the likelihood of achieving negative margins, improving long-term survival rates.[16]

d) Objectivity: AI eliminates inter-observer variability inherent in histopathological assessment.[5] Histopathological evaluation, including frozen section analysis, is subject to inter-observer variability, as different pathologists may interpret the same slide differently based on their experience, training, or subjective judgment.[11] This variability can lead to inconsistent margin assessments, affecting surgical decisions and patient outcomes. AI, by contrast, provides an objective, standardized approach to margin analysis. Once trained, AI models apply consistent criteria across all samples, eliminating human bias and variability.[15]DL models use predefined features and thresholds to classify tissue as malignant or benign, ensuring reproducibility regardless of the user or setting.[17] This objectivity is particularly valuable in resource-limited settings, where access to highly trained pathologists may be limited. Additionally, AI can be audited and refined to maintain consistency, further enhancing its reliability over time.[18]

e) Integration: AI can combine multiple modalities (e.g., HSI+OCT) for enhanced precision.[14] AI excels at integrating data from multiple imaging modalities, such as HSI, OCT, fluorescence imaging, or intraoperative ultrasound, to provide a more comprehensive and precise assessment of margins.[6,11,15] Each modality offers unique insights—HSI captures spectral signatures of tissue, OCT provides high-resolution structural details, and fluorescence highlights molecular markers of malignancy.[13,17] By fusing these data streams, AI creates a multidimensional view of the margin, improving diagnostic accuracy beyond what any single modality can achieve.[5]

Table 1: AI Technologies in Intraoperative Margin Assessment

Technology	AI/ML Method(s) Used	Key Capabilities/Benefits	Performance Metrics	Limitations
Machine Learning & Deep Learning	ML, DL, Convolutional Neural Networks (CNNs) [4]	Classifies tissues (malignant/benign) from imaging(e.g., CT, MRI, histopathological images) predicts margin status from pre-op imaging[5]	>90% accuracy in distinguishing cancerous from normal oral tissues (histopathological images) [6]	Requires preoperative imaging for training[6]
Hyperspectral Imaging (HSI)	Support Vector Machines (SVMs), CNNs	Captures unique spectral signatures; maps tumor boundaries intraoperatively	91% sensitivity, 87% specificity in detecting oral cancer margins[6]	Non-invasive and rapid processing (seconds) make it ideal for real-time assessment[7]
Optical Coherence Tomography (OCT)	DL, CNNs[8]	High-resolution, cross-sectional imaging of tissue microstructure; differentiates tissues[6]	93% accuracy in identifying positive margins in oral squamous cell carcinoma [9]	Depth penetration (1-2 mm); requires specialized probes[10]
Raman Spectroscopy	Random Forests, Neural Networks[6]	Measures molecular vibrations for biochemical differences; detects tumor margins	>95% accuracy in ex vivo studies; 89% sensitivity in oral cancer resections[11,12]	Requires direct tissue contact, potentially slowing comprehensive margin evaluation[13]
Augmented Reality (AR) & Fluorescence-Guided Surgery	AI-driven AR, ML algorithms	AR overlays tumor boundaries onto surgical fields; ML processes fluorescence signals[14]	AR improved clear margin rates by 15% ,92% accuracy in margin detection[14] (fluorescence)	Dependent on preoperative/intraoperative data quality

Limitations and Challenges

Integration of AI into intraoperative margin assessment for oral cancer holds transformative potential, but several limitations and challenges hinder its widespread adoption. Below, we elaborate on the key obstacles:

a) Training Data

AI models, particularly those employing ML and DL, rely on large, high-quality, annotated datasets to achieve robust performance. In the context of oral cancer, acquiring such datasets is challenging due to the disease's heterogeneity, which encompasses diverse histological subtypes, anatomical locations, and molecular profiles.[19] The scarcity of standardized, publicly available datasets limits model training and validation. Moreover, annotation requires expert pathologists to label tissue samples as malignant or benign, a process that is time-consuming and prone to inter-observer variability. [15]

b) Generalizability

The generalizability of AI models is a significant concern, as models trained on specific populations, imaging modalities, or clinical settings may not perform reliably in diverse contexts.[20] . For instance, a model developed using HSI data from a single institution may underperform when applied to different HSI systems with varying spectral resolutions or calibration protocols.[8] Similarly, demographic factors, such as ethnicity or socioeconomic status, can influence tissue characteristics and disease presentation, potentially introducing bias if training data lack diversity.[20] Without addressing these issues, AI tools risk limited applicability in global healthcare settings.

c) Cost and Accessibility

Advanced imaging technologies integral to AI-driven margin assessment, such as HSI, OCT, and Raman spectroscopy, are costly to acquire, maintain, and operate.[21] These systems require specialized hardware, trained personnel, and regular calibration, posing financial barriers for low-resource hospitals, particularly in developing countries. While open-source AI frameworks and portable imaging devices are emerging, their performance often lags behind proprietary systems. Bridging this accessibility gap is critical to ensuring equitable adoption of AI technologies in oral cancer surgery.[22]

d) Intraoperative Integration

Real-time AI deployment in the operating room demands seamless integration with existing surgical workflows, which poses technical and logistical challenges.[23] AI systems must process imaging data and deliver margin assessments within seconds to avoid disrupting surgery, necessitating robust hardware (e.g., high-speed processors) and software (e.g., optimized algorithms). Compatibility issues between AI platforms and surgical equipment, such as microscopes or endoscopes, can further complicate integration. Additionally, surgeons and operating room staff require training to effectively use AI tools, which may face resistance due to unfamiliarity or skepticism. Developing user-friendly interfaces and conducting interdisciplinary training programs are critical to ensuring that AI enhances, rather than hinders, surgical efficiency.[23]

e) Regulatory Hurdles

The clinical deployment of AI tools is subject to stringent regulatory oversight to ensure patient safety and efficacy. Regulatory bodies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), require rigorous validation through clinical trials to demonstrate that AI systems perform consistently across diverse patient populations and clinical scenarios.[24] This process is time-consuming and resource-intensive, often delaying the translation of promising AI tools from research to practice.[25] Developing standardized validation protocols and interpretable AI frameworks is essential to expedite regulatory+ regulatory approval.[20]

Present Application and Future evolution

A 2021 multicenter study evaluated DL-based HSI in 102 oral cancer patients, reporting 90% accuracy in margin assessment, reducing positive margin rates from 12% to 4%.[26] Similarly, a 2022 trial using OCT with CNNs in 78 patients achieved 94% sensitivity, with a 10% improvement in local recurrence-free survival at 1 year.[27] Raman spectroscopy, tested in 65 patients, showed 91% accuracy, though its contact-based nature limited comprehensive margin coverage.[22] AR-guided surgery, trialed in 50 patients, increased clear margin rates by 18%, with no increase in operative time.[28]

Future Directions

a) Multimodal AI: Combining HSI, OCT, and Raman spectroscopy with DL could achieve near-100% accuracy by leveraging complementary data. [15]

b) Real-Time Decision Support: AI-driven AR systems could guide surgeons dynamically, adjusting resection plans based on intraoperative findings. [18]

c) Automated Pathology: AI could replace frozen sections entirely, integrating with robotic surgery for autonomous margin assessment. [17]

d) Personalized Models: Patient-specific AI models, trained on preoperative imaging and genetic data, could optimize margin prediction . [11]

e) Global Accessibility: Cloud-based AI platforms could democratize access, enabling low- resource centers to adopt advanced margin assessment.[24]

Future AI for oral cancer margin assessment will integrate multimodal deep learning (HSI, OCT, Raman, genomics, proteomics) with integrated learning for enhanced accuracy.

Real-time AR will guide surgery with submillimeter precision. Quantum computing may accelerate analysis. Nanosensors could detect microscopic residual disease. These advancements aim for personalized, precise surgery, reducing recurrence.

Recommendations

AI is transforming intraoperative margin assessment in oral cancer surgery, offering superior accuracy, speed, and comprehensiveness compared to traditional methods. HSI, OCT, Raman spectroscopy, and AR, powered by ML and DL, enable real-time, precise margin delineation, reducing recurrence risk and improving outcomes. Despite challenges like data requirements and costs, ongoing advancements in multimodal AI and integration promise to make these tools indispensable. Future research should focus on large-scale validation, cost reduction, and seamless intraoperative deployment to maximize clinical impact.

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