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PREOPERATIVE ASSESSMENT OF RECURRENT HEAD AND NECK CANCER RESECTABILITY: RADIOMICS, ARTIFICIAL INTELLIGENCE, AND MOLECULAR BIOMARKERS

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ABSTRACT

Introduction. Recurrent head and neck squamous cell carcinoma is difficult to assess after chemoradiotherapy because fibrosis, edema, and distortion of anatomical landmarks may obscure viable tumor.

Aim. To summarize the roles of computed tomography, magnetic resonance imaging, positron emission tomography, radiomics, artificial intelligence, and molecular biomarkers in preoperative assessment of resectability and complication risk.

Materials and methods. A narrative synthesis of 39 verified and clinically relevant publications was performed. Sources were grouped by imaging modality, radiomic modeling, molecular phenotype, and validation requirements.

Results. Conventional imaging remains essential for defining tumor extent, but specificity decreases in the presence of post-treatment change. Radiomic features may capture tumor heterogeneity, and radiogenomic studies have reported associations with human papillomavirus status and molecular subtypes. Clinical translation remains limited by heterogeneous imaging protocols, overfitting, inadequate external validation, and the lack of prospective evidence that model-assisted decisions improve surgical outcomes.

Conclusion. Standardized multiparametric imaging should be integrated with clinical variables and validated molecular biomarkers. Until prospectively evaluated, these models should support rather than replace multidisciplinary decisions regarding salvage surgery.

KEYWORDS: artificial intelligence; diagnostic imaging; head and neck cancer recurrence; molecular biomarkers; radiogenomics; radiomics.

INTRODUCTION

Recurrent head and neck tumors pose a major clinical challenge because post-treatment anatomy is altered and patterns of local recurrence are highly variable. These factors may delay the recognition of unresectable disease [3, 4]. Conventional imaging remains the diagnostic foundation, but scar tissue, edema, and fibrosis may obscure the true tumor boundary and complicate assessment of critical structures [5, 6]. Radiomics and artificial intelligence (AI) can convert medical images into quantitative biomarkers that potentially reflect tumor microarchitecture, heterogeneity, and invasive behavior [23-26].

The broader salvage-treatment literature includes reirradiation, proton therapy, intraoperative radiotherapy, and stereotactic approaches [1, 2, 7, 39]. These studies emphasize the importance of patient selection and accurate target definition, although they do not by themselves validate imaging-based prediction of surgical resectability.

Radiomic models may also contribute to the prediction of postoperative outcomes, including bleeding, wound complications, and functional impairment. Machine-learning algorithms can identify multivariable patterns that may not be apparent on visual inspection, thereby supporting personalized planning of salvage surgery [24-27]. Nevertheless, most published models address prognosis, treatment response, or molecular phenotype rather than technical surgical resectability. Their results therefore cannot be transferred directly to operative decision-making.

Radiogenomics, which relates quantitative imaging features to genetic, transcriptomic, viral, or other molecular characteristics, is particularly relevant to Genetics and Molecular Research. In head and neck squamous cell carcinoma (HNSCC), imaging models have been associated with human papillomavirus (HPV)/p16 status and molecular subtypes [9, 10, 13, 38]. Whether these associations improve assessment of recurrent tumor resectability remains uncertain.

This review aimed to summarize the role of diagnostic imaging, radiomics, and AI in assessing the resectability of recurrent head and neck tumors; examine the contribution of molecular biomarkers; and define the methodological requirements for clinical validation.

MATERIALS AND METHODS

This work was designed as a narrative review. The analysis comprised 39 verified and clinically relevant publications from the bibliography of the source manuscript. The publications were organized into five domains: post-treatment imaging; quantitative assessment of local invasion; machine learning and outcome prediction; hybrid imaging; and radiogenomic associations with HPV/p16 status and molecular subtypes. Information on imaging modality, intended clinical task, biomarker type, validation approach, and major limitations was extracted qualitatively. Because the source manuscript did not document the databases searched, search dates, search strings, or formal eligibility criteria, this article should not be presented as a systematic review. The authors must add the actual literature-search procedure before submission.

Limitations of post-treatment imaging

Interpretation of computed tomography (CT) and magnetic resonance imaging (MRI) after treatment is complicated by fibrosis, edema, necrosis, and tissue deformation. These findings may resemble recurrent tumor or conceal its margins [16, 20, 23]. CT provides rapid assessment of bone, airways, and major vascular relationships but offers limited soft-tissue contrast. MRI provides superior soft-tissue characterization and diffusion-weighted imaging may improve tissue differentiation, although inflammatory and fibrotic changes remain difficult to interpret.

18F-fluorodeoxyglucose positron emission tomography combined with CT (18F-FDG PET/CT) is sensitive for metabolically active recurrence and occult distant disease [10, 21]. Its specificity may be reduced by inflammation and infection. The timing of imaging is therefore important, and a positive result should be interpreted in the context of morphology, symptoms, endoscopy, and biopsy whenever feasible. Published surveillance studies also disagree on the benefit of repeated routine imaging after a negative early PET/CT examination [8, 21, 34].

Thus, no single modality reliably distinguishes all recurrent tumors from benign post-treatment changes. Resectability should be assessed by integrating complementary imaging findings with the expected surgical approach and patient-specific clinical factors.

Radiomics and quantitative assessment of resectability

Radiomics derives quantitative descriptors of tumor shape, first-order intensity, and higher-order texture from standard images. Machine-learning models can combine these variables to reveal patterns that are not readily visible to radiologists [23, 26, 28]. For recurrent HNSCC, such features could quantify irregular margins, spatial heterogeneity, or relationships with adjacent tissues. However, a potential association with invasion is not equivalent to validated prediction of resectability.

A clinically meaningful model must predict a clearly defined surgical endpoint, such as the probability of an R0 resection, carotid artery encasement, skull-base invasion, prevertebral fascia involvement, or a specified postoperative complication. Many cited studies instead predicted survival, local control, HPV status, or treatment response [9, 15, 21, 27, 35, 36]. These findings support the biological relevance of radiomics but provide only indirect evidence for salvage-surgery planning.

Radiogenomics and molecular phenotypes

CT-derived radiomic features have been investigated as noninvasive markers of HPV or p16 status in oropharyngeal squamous cell carcinoma [9, 13, 38]. Multimodal signatures have also been associated with molecular characteristics and HNSCC subtypes [10]. These observations support the concept that an image can act as a spatial phenotype of tumor biology and may complement tissue sampling, particularly when recurrent lesions are heterogeneous or difficult to biopsy.

Related studies have linked HPV status with imaging phenotypes and clinical outcome, while radiomic prognostic modeling has also been explored in other head and neck or thyroid malignancies [12, 14]. Such evidence illustrates the cross-tumor potential of quantitative imaging but also underlines the need for disease- and endpoint-specific validation.

Nevertheless, HPV status, molecular subtype, and technical resectability are distinct endpoints. A marker may be prognostic without identifying invasion of a surgically critical structure. Studies in recurrent disease should therefore correlate radiogenomic signatures with intraoperative findings, histopathological margin status, and specific postoperative outcomes. Molecular data should be obtained using standardized assays, and temporal discordance between the primary tumor and recurrence must be considered.

Artificial intelligence and prediction of surgical complications

AI models can process larger numbers of clinical and imaging variables than conventional visual assessment and may identify complex interactions among risk factors [23-27, 35, 36]. Combining PET/CT or CT radiomics with machine-learning classifiers has improved risk stratification in several HNSCC cohorts [9, 21, 27]. However, evidence for prediction of complications after salvage surgery remains limited. Previous radiation dose, interval since treatment, nutritional status, vascular involvement, reconstructive method, and comorbidity should be incorporated alongside image-derived features. Claims of clinical utility require comparison with multidisciplinary assessment and demonstration of incremental benefit.

Hybrid imaging technologies

Integrated PET/MRI combines metabolic information with high soft-tissue contrast and multiparametric MRI, including diffusion-weighted sequences. It may improve delineation of local recurrence in anatomically complex regions while reducing

the radiation exposure associated with repeated CT. Spectral CT can provide material-specific information that may help distinguish enhancing tumor from treatment-related change. These approaches are promising for preoperative assessment, but availability, acquisition time, artifacts, and limited multicenter evidence restrict routine use. Their value should be tested against clinically relevant surgical reference standards.

Standardization, validation, and clinical implementation

Radiomic features are sensitive to scanner type, acquisition parameters, reconstruction, segmentation, preprocessing, and image noise [17, 19, 22, 29, 31, 33, 37]. Standardization of the complete workflow is therefore essential. Multicenter external validation is more informative than random splitting of a small single-center cohort, particularly in patients previously treated with radiotherapy, whose imaging appearances are highly heterogeneous [23, 24, 30].

Major risks of bias include retrospective sampling, small cohorts, multiple feature testing, outcome imbalance, overfitting, and data leakage between training and test sets. Studies should prespecify endpoints, separate all preprocessing and feature-selection steps within the training data, report calibration as well as discrimination, and evaluate clinical usefulness using decision-analytic methods [18, 24, 30, 37]. Transparent reporting and reproducible feature definitions are prerequisites for regulatory assessment and clinical adoption.

Feature-selection methods must also account for censoring when time-to-event outcomes are analyzed [11]. For local salvage procedures, reproducible target delineation and the relationship between automated segmentation and treatment margins remain clinically relevant [32].

A practical decision-support system should combine standardized imaging, radiomic features, anatomical criteria, previous treatment data, and validated molecular biomarkers. Its output should be interpretable and discussed by radiologists, nuclear-medicine physicians, surgeons, radiation oncologists, pathologists, and molecular specialists. Prospective impact studies must establish whether use of the model reduces futile operations or complications without denying potentially curative surgery.

CONCLUSION

Radiomics and AI can extend conventional imaging in recurrent head and neck cancer, but current evidence for direct determination of surgical resectability is limited. Integration of quantitative imaging with clinical and molecular data, including HPV/p16 status and validated molecular subtypes, is a biologically plausible strategy. Future studies require prospective multicenter design, independent external validation, and surgical endpoints such as intraoperative invasion, margin status, and complication rates. Until such evidence is available, algorithmic predictions should complement rather than replace multidisciplinary judgment.

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