



Radiomics and Machine Learning in the Early Detection of Oral Potentially Malignant Disorders (OPMD) Transition to Oral Squamous Cell Carcinoma (OSCC)

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Abstract

Introduction: Early detection of malignant transformation in oral potentially malignant disorders (OPMDs) is vital for improving survival in oral squamous cell carcinoma (OSCC). Conventional diagnostics, including histopathology, are invasive and subject to variability. Radiomics, which extracts quantitative features from imaging data, combined with machine learning (ML) and deep learning (DL), offers reproducible, non-invasive biomarkers to complement clinical assessment.

Discussion: Radiomics workflows involve image acquisition, segmentation, feature extraction, and predictive modeling. Applied across modalities such as CT, MRI, PET, ultrasound, autofluorescence, and optical coherence tomography (OCT), radiomic features integrated with ML algorithms enable risk stratification, guided biopsies, and longitudinal monitoring of OPMDs. Emerging technologies, including hyperspectral imaging, Raman spectroscopy, digital pathology, and liquid biopsy integration, further enhance diagnostic potential. Recent advances in software and AI platforms—such as PyRadiomics, 3D Slicer, CaPTk, MONAI, AutoRadiomics, cloud AI, federated learning, and explainability frameworks—are accelerating clinical translation. However, challenges persist due to heterogeneous data, small sample sizes, and segmentation variability. Solutions include harmonization techniques, data augmentation, robust automatic segmentation, and adherence to reporting standards.

Conclusion: Radiomics and AI-driven methods show strong promise for early, non-invasive detection of OPMD progression to OSCC. While standardization, reproducibility, and clinical validation remain barriers, advances in AI ecosystems and collaborative, multi-institutional research are paving the way toward precision diagnostics and clinical implementation.

Keywords: Radiomics; Machine Learning; Oral Potentially Malignant Disorders; Oral Squamous Cell Carcinoma; Artificial Intelligence; Imaging Biomarkers; Early Detection

Abbreviation

AI: Artificial Intelligence; AutoML: Automated Machine Learning; CaPTk: Cancer Imaging Phenomics Toolkit; CLAIM: Checklist for Artificial Intelligence in Medical Imaging; CNN: Convolutional Neural Network; CT: Computed Tomography; DL: Deep Learning; HER: Electronic Health Record; FDG: Fluorodeoxyglucose; GLRLM: Gray Level Run Length Matrix; GLSZM: Gray Level Size Zone Matrix; GLCM: Gray Level Co-occurrence Matrix; GUI: Graphical User Interface; H&E: Hematoxylin and Eosin; HIS: Hyperspectral Imaging; IBSI: Image Biomarker Standardisation Initiative; LASSO:

Least Absolute Shrinkage and Selection Operator; LoG: Laplacian of Gaussian; ML: Machine Learning; MONAI: Medical Open Network for AI; MRI: Magnetic Resonance Imaging; NBI: Narrow Band Imaging; OCT: Optical Coherence Tomography; OPMD: Oral Potentially Malignant Disorder; OSCC: Oral Squamous Cell Carcinoma; PACS: Picture Archiving and Communication System; PCA: Principal Component Analysis; PET: Positron Emission Tomography; ROI: Region of Interest; SHAP: SHapley Additive exPlanations; SOP: Standard Operating Procedure; SVM: Support Vector Machine; TRIPOD-AI:

Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis Using AI; US: Ultrasound; WSI: Whole Slide Imaging; XAI: Explainable Artificial Intelligence

Introduction

Oral squamous cell carcinoma (OSCC) is responsible for the vast majority of oral cancers worldwide and carries substantial morbidity and mortality, in part because many cases are diagnosed at an advanced stage [1]. Early identification of lesions at high risk of malignant transformation — oral potentially malignant disorders (OPMDs) such as leukoplakia, erythroplakia, oral submucous fibrosis and oral lichen planus — is therefore a priority for reducing OSCC burden [2]. Histopathology remains the gold standard for diagnosing dysplasia but suffers from sampling error and inter-observer variability; moreover, biopsies are invasive and not optimal for longitudinal surveillance [3].

Radiomics translates medical images into quantitative descriptors that reflect tissue composition, architecture and heterogeneity. When combined with ML and DL, these descriptors can generate predictive models for lesion classification, risk stratification and guidance for biopsy sampling. Radiomics has matured in multiple oncologic domains and is rapidly being adapted to oral mucosal disease and early OSCC detection [4-6]. This review provides a structured synthesis of the field, with emphasis on modalities, feature types, ML strategies, software/platforms, limitations and future directions, followed by a practical table summarizing recent advances.

Radiomics: concept and standardized workflow

Radiomics is founded on the premise that imaging contains quantifiable information beyond human interpretation. A reproducible radiomics pipeline comprises:

- Image acquisition and harmonization — consistent protocols or harmonization techniques to mitigate inter-scanner differences [7].
- Segmentation — defining the region of interest (ROI) manually, semi-automatically or automatically; segmentation variability is a major source of downstream variability [8].
- Preprocessing — resampling, intensity normalization and denoising [9].
- Feature extraction — first-order (histogram), shape, texture (GLCM, GLRLM, GLSZM), and higher-order features (wavelets, Laplacian of Gaussian) [10].

- Feature selection/reduction — LASSO, PCA, mutual information, recursive feature elimination to avoid overfitting [11].
- Model training and validation — classical ML (SVM, random forest, gradient boosting) or DL (CNNs) with nested cross-validation and preferably external testing [12].
- Explainability and calibration — SHAP/LIME and calibration plots to support clinical trust and decision thresholds [13].

Adhering to reporting standards (Image Biomarker Standardisation Initiative, TRIPOD-AI, CLAIM) improves reproducibility and comparability across studies [7,14].

Imaging modalities and their radiomic utility in OPMD

Optical modalities (clinical photography, autofluorescence, NBI, OCT)

Optical imaging is directly applicable to superficial oral mucosa. Clinical photographs and wide-field imaging capture macroscopic features; DL can triage lesions for referral. Autofluorescence and narrow band imaging (NBI) reveal metabolic and vascular changes; quantitative texture analysis reduces subjective interpretation. OCT provides subsurface microstructural imaging with near-histologic resolution; radiomic features from OCT can quantify epithelial thickness, signal heterogeneity and epithelial-stromal interface disruption associated with dysplasia [15-17].

Hyperspectral imaging (HSI), Raman spectroscopy, multiphoton microscopy

HSI records spectral signatures of tissue and enables biochemical discrimination (hemoglobin, collagen, keratin). Raman spectroscopy detects molecular vibrational fingerprints; multiphoton microscopy visualizes collagen and cellular autofluorescence. Radiomic and ML analysis of data from these modalities can identify biochemical alterations in OPMDs preceding morphological change [18-20].

Cross-sectional and metabolic imaging (CT, MRI, PET)

CT and MRI provide anatomical context and are more commonly used in staging; however, radiomic features from these modalities have prognostic value in head and neck oncology and can be applied to complex or deep lesions. PET radiomics (e.g., ^{18}F -FDG) captures metabolic heterogeneity that may correlate with aggressive biology [21,22].

Digital pathology/pathomics

Whole-slide imaging (WSI) of H&E sections enables computational pathomics: extraction of nuclear morphology, spatial arrangement, stromal features and immune cell patterns. Pathomics models have shown predictive power for malignant transformation in oral epithelial dysplasia and often augment or outperform conventional grading [23,24].

Machine learning strategies and deep learning paradigms

Traditional ML

After feature engineering, classical supervised algorithms (random forest, SVM, gradient boosting machines) are commonly used for OPMD classification and risk modelling. They provide relative interpretability, work well with limited data and allow feature-importance analysis [11,25].

Deep learning

Deep convolutional neural networks (CNNs) can learn hierarchical representations directly from images (clinical photos, autofluorescence, OCT, WSI). Transfer learning using pre-trained architectures (ResNet, EfficientNet) mitigates small dataset issues. Hybrid models combining handcrafted radiomic features with CNN outputs often achieve the best performance [19,26].

Model validation and generalizability

Robust validation requires nested cross-validation and, crucially, external multi-center testing. Federated learning offers a path to pooling model knowledge without sharing raw data, addressing privacy and legal barriers [27].

Explainability and clinical integration

Explainable AI (XAI) methods (SHAP, Grad-CAM, LIME) help visualize which features or image regions drive predictions, aiding clinician acceptance and facilitating regulatory submission [13].

Clinical applications and demonstrated use-cases

- Screening and triage — CNNs on clinical photographs or wide-field imaging can flag suspicious lesions for specialist referral, a scalable approach for low-resource settings [15].
- Risk stratification of OPMDs — radiomic signatures stratify lesions into low versus high malignant potential, informing surveillance intervals or early intervention [17].

- Biopsy guidance — radiomic heatmaps and OCT-derived maps can localize areas with most severe architectural disruption to target biopsy and reduce sampling error [23].
- Longitudinal monitoring (delta-radiomics) — tracking radiomic changes over time (delta features) improves early detection of progression [22].
- Prognostication post-transformation — imaging phenotypes correlate with recurrence risk and treatment response following OSCC diagnosis; radiomics aids personalized management [21,24].

Recent software, platforms, and emerging AI ecosystems

Advances in software and computational ecosystems have significantly lowered the barriers to radiomics research and facilitated clinical translation. Among the most widely adopted tools is PyRadiomics, an open-source Python library that provides standardized radiomic feature extraction and is compliant with the Image Biomarker Standardisation Initiative (IBSI), making it highly reliable for reproducible workflows [26]. Similarly, the 3D Slicer radiomics extension offers modular pipelines for visualization, segmentation, and feature extraction within a graphical user interface, which makes it particularly suitable for integration into clinical research environments [28]. The Cancer Imaging Phenomics Toolkit (CaPTk) provides advanced analytics capabilities, combining radiomics with machine learning modules; although developed primarily for neuro-oncology, it is readily adaptable to head and neck imaging studies [27].

In parallel, deep learning (DL) applications have been accelerated by platforms such as MONAI (Medical Open Network for AI), a PyTorch-based framework specifically optimized for medical imaging, offering community-driven best practices and reproducible training recipes [28]. The emergence of AutoRadiomics and automated machine learning (AutoML) platforms has further streamlined development by automating feature selection, hyperparameter tuning, and validation, thereby reducing coding requirements and enabling broader adoption [29,30]. For scalability and deployment, cloud-based AI platforms including Google Cloud AutoML, AWS SageMaker, and Microsoft Azure ML provide robust computational infrastructure for training large-scale models and hosting real-time inference in clinical settings [29].

Privacy and data security remain critical in multi-institutional collaborations, and here federated learning frameworks such as Flower and TensorFlow Federated enable decentralized model training without centralizing patient data, addressing both regulatory and ethical concerns [27]. To improve transparency and clinical adoption, explainability tools such as SHAP, LIME, and Grad-CAM provide interpretable outputs that enhance clinician trust and are increasingly demanded in regulatory evaluations [13]. Collectively, these software platforms and AI ecosystems support reproducible radiomics pipelines, from image ingestion and harmonization through feature analysis and model deployment, thereby accelerating multi-center research and facilitating pilot clinical translation.

Emerging technologies and multi-modal integration

- **Hyperspectral imaging + radiomics:** Spectral signatures coupled with texture features can improve biochemical discrimination of dysplasia [18].
- **Raman spectroscopy and multiphoton microscopy:** Molecular-level imaging fed to ML models can identify early carcinogenic biochemical changes [19,20].
- **Liquid biopsy + radiomics:** Integrating circulating tumor DNA, exosomal RNA or salivary biomarkers with image features produces stronger predictive models (multi-omics fusion) [23,25].
- **Pathomics + radiomics (cross-scale models):** Fusing WSI features with in-vivo imaging provides comprehensive phenotyping from molecule to organ [23,24].
- **Delta-radiomics and temporal modeling:** Sequential imaging captures trajectory of lesion evolution and improves early detection sensitivity [22].

Limitations, pitfalls, and strategies to address them

Despite the promising potential of radiomics and machine learning in predicting OPMD progression to OSCC, several limitations and pitfalls must be acknowledged. A major challenge is the heterogeneity of imaging data and acquisition protocols across centers, which can significantly affect feature reproducibility.

To mitigate this, harmonization techniques such as ComBat and the adoption of standardized acquisition SOPs have been recommended [7]. Another critical issue is the reliance on small and often imbalanced datasets, which increases the risk of model overfitting and limits generalizability. Strategies such as data augmentation, transfer learning, and federated learning have been employed to increase effective sample size and model robustness [26,27]. Segmentation variability, both inter- and intra-observer, also remains a key obstacle, as manual segmentation introduces subjectivity and impacts feature stability. The development of robust automatic segmentation algorithms, alongside quantification of inter-rater variability in model reporting, is essential to overcome this [8].

Reproducibility and reporting standards further present challenges in this rapidly evolving field. To address these, adherence to guidelines such as the Image Biomarker Standardisation Initiative (IBSI), Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis using AI (TRIPOD-AI), and the Checklist for Artificial Intelligence in Medical Imaging (CLAIM) is strongly encouraged, along with sharing of code, models, and datasets whenever feasible [14]. Finally, regulatory and ethical considerations must be addressed before translation into clinical practice. Transparent validation pipelines, systematic bias assessment across demographic groups, and prospective clinical trials are necessary to demonstrate real-world clinical impact and ensure safe, equitable deployment of AI-based radiomic tools [13,30].

Future Directions

To move radiomics and ML from research to routine OPMD care, priorities include: building large, well-annotated multi-center cohorts with longitudinal outcomes; federated consortia to protect privacy while enabling model generalization; prospective impact trials demonstrating clinical utility (reduced missed transformations, optimized biopsy strategies, improved survival); and development of clinician-centric interfaces with clear explainability and integration into electronic health records/PACS. Radiogenomic and multi-omic models that combine imaging, pathology and circulating biomarkers are particularly promising for personalized surveillance [23-25].

Table 1: Recent advances: technologies, applications and representative references.

Advance/Platform	Modality/Data	Primary Application (s)	Key advantages	Representative refs
PyRadiomics	CT/MRI/PET/OCT/US (feature extraction)	Standardized radiomic feature extraction	Open-source, IBSI-aligned, widely used	[26]
3D Slicer (Radiomics ext.)	Multi-modal imaging	Segmentation → radiomics pipeline	GUI, modular, extensible	[28]
CaPTk	MRI/CT	Quantitative imaging analytics and ML	Neuro/oncology toolkit, radiogenomic modules	[27]
MONAI	Medical imaging DL	Deep learning model development	PyTorch-based, reproducible workflows	[28]
AutoRadiomics/AutoML	Multi-modal	Automated feature selection and model tuning	Lowers technical barrier, faster prototyping	[29,30]
Federated Learning frameworks	Multi-institutional image datasets	Collaborative model training without data sharing	Privacy preserving, improves generalizability	[27]
SHAP/LIME/Grad-CAM (XAI)	Any ML/DL model	Explainability and feature attribution	Clinician interpretability, auditability	[13]
OCT + Radiomics	OCT	Subsurface dysplasia detection and biopsy guidance	Near-histologic detail, non-invasive	[15,19]
Hyperspectral Imaging + ML	HSI	Biochemical discrimination of dysplasia	Spectral specificity, non-contact	[18]
Raman spectroscopy + ML	Raman	Molecular fingerprinting for early changes	High molecular specificity	[19]
Pathomics (WSI + DL)	Digital histology	Predict malignant transformation from biopsy	High predictive power, interpretable histologic features	[23,24]
PET Radiomics	¹⁸ F-FDG PET	Metabolic heterogeneity → risk stratification	Functional imaging adds biology	[21]
Delta-radiomics (temporal)	Serial imaging	Early detection of dynamic change	Captures lesion evolution	[22]

Conclusion

Radiomics and machine learning offer objective, non-invasive approaches for early detection and risk stratification of OPMDs with the potential to reduce OSCC incidence via earlier intervention. Progress in imaging modalities, software platforms, federated learning and explainable AI is accelerating translation. Realizing clinical impact requires rigorous external validation, standardized workflows, multi-center collaboration, and prospective demonstration of improved patient outcomes.

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