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Artificial Intelligence in Oral and Maxillofacial Oncology: AI-Driven Histopathological, Imaging, and Surgical Insights into Oral Squamous Cell Carcinoma

Cristian Niky Cumpătă
Titu Maiorescu University, Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Associate Professor, Bucharest, Romania.
nikycumpata@yahoo.com,
https://orcid.org/0000-0001-5414-0031

Anca Mihaela Predescu
University of Medicine and Pharmacy of Craiova, Faculty of Dentistry, Histology. Citology Department, Lecturer, Craiova, Romania. medpredes@yahoo.com,
https://orcid.org/0009-0007-6297-3747

Larisa Pătru
University of Medicine and Pharmacy of Craiova, Faculty of Medicine, Lecturer, Craiova, Romania. larisa.patru@umfcv.ro,
https://orcid.org/0000-0002-6897-3381

Maria Totan
Lucian Blaga University of Sibiu, Faculty of Medicine, PhD student, Sibiu, Romania. maria.totan@ulbsibiu.ro,
https://orcid.org/0000-0002-9601-7303

Cristina Maria Munteanu
University of Medicine and Pharmacy of Craiova, Department of Oral and Maxillofacial Surgery, Faculty of Dental Medicine, Lecturer, Craiova, Romania. cristina.munteanu@umfcv.ro,
https://orcid.org/0009-0004-0743-2313

Oprea Valentin Bușu
University of Craiova, Department of Education and Communication Sciences, Faculty of Letters, Lecturer, Craiova, Romania. valentin_busu@yahoo.com,
https://orcid.org/0000-0001-5917-8821

Ilona Mihaela Liliac
University of Medicine and Pharmacy of Craiova, Faculty of Medicine, Histology. Citology Department, Lecturer, Craiova, Romania. ilona.mihaela.liliac@gmail.com,
https://orcid.org/0000-0002-4403-7361

Abstract: *Artificial intelligence (AI) is rapidly transforming the medical oncology, by providing new tools for early diagnosis and personalized treatment planning. In mandibular oncology, where malignant transformation and metastatic progression can drastically alter prognosis, AI-driven systems show great promise in enhancing clinical decision-making. Convolutional neural networks and deep learning algorithms have already demonstrated high accuracy in analyzing imaging datasets, including CT scans and histopathological slides, for the detection of subtle changes that may indicate malignant transformation of initially benign lesions. These tools also aid in identifying early metastatic spread, allowing for timely intervention. One of the most aggressive head and neck cancers, oral squamous cell carcinoma (OSCC) usually affects the mandible and causes extensive anatomical disruption, neurological impairments, and functional deficits in speech, mastication, and facial symmetry. This article presents clinical and histopathological data on malignant lesions of the mandibular bone, primarily oral squamous cell carcinoma (OSCC). Tumours primarily affected the mandibular body and ramus, often causing facial asymmetry, tooth mobility, and bone loss. Histologically, keratin pearls and spindle-shaped atypical cells were typical characteristics. Neurological involvement from perineural invasion frequently led to pain, numbness, and impaired oral function. In addition to the complex consequences of mandibular cancers, such as their anatomical, functional, and psychological effects, the study underscores the importance of multidisciplinary treatment and rehabilitation. Our paper presents how new methods for improving the precision and effectiveness of oral oncology diagnosis have been made possible by developments in artificial intelligence (AI), especially deep learning approaches. By recognising both cellular and structural atypia, convolutional neural networks (CNNs) have shown excellent performance in the classification of histopathological images. The distinction between benign, dysplastic, and malignant oral lesions is further enhanced by hybrid techniques that blend deep and texture-based features. AI-assisted radiomics has shown promise in diagnostic imaging by detecting high-dimensional, subtle characteristics in CT, MRI, and ultrasound scans that are frequently impossible to interpret visually. According to analysed studies, these techniques can improve the identification of lymph node metastases and offer accurate risk assessment for oral malignancies. Further encouraging their inclusion into the oral oncology workflow, machine learning models have attained diagnostic accuracies that surpass standard radiological assessments by merging image texture analysis with clinical data. A triadic viewpoint is provided by integrating AI into mandibular oncology: (1) imaging-based tumour growth and metastasis detection, (2) histopathological evaluation of malignant potential, and (3) assessment of neurological outcomes following surgery. Also, this article presents a case study from the University of Craiova, guide surgical excision, and assess both histological progression and postoperative functional impact. AI technologies' ability to support individualized treatment plans, enable earlier diagnoses, and enhance clinical judgment is becoming more and more clear as they develop—especially in anatomically and neurologically complex areas like the mandible. In conclusion, AI represents a powerful ally in mandibular oncology, bridging imaging, histopathology, and neurological evaluation, and paving the way for more precise, patient-centered care.*

Keywords: *artificial Intelligence; psychotherapy; responsible AI; explainable AI (XAI); shared decision making (SDM); electronic health records (EHR); harm Prevention (HP); mental health; ethical framework; public health systems; clinical decision support; digital mental health.*

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Elena Cristina Andrei*
University of Medicine and Pharmacy of Craiova, Faculty of Dentistry, Histology. Citology Department, Lecturer, Craiova, Romania.
Corresponding author: andreicristina2201@gmail.com, tel. +40.767924788, https://orcid.org/0009-0008-1581-8928

Marina Amarascu
University of Medicine and Pharmacy of Craiova, Faculty of Dentistry, Tooth Morphology Department, Lecturer, Craiova, Romania.
https://orcid.org/0000-0002-3394-1486

Ciprian Laurențiu Pătru
University of Medicine and Pharmacy of Craiova, Faculty of Medicine, Department of Gynecology, Lecturer, Craiova, Romania.
ciprian.patru@umfcv.ro, https://orcid.org/0000-0003-3672-5989

These authors contributed equally.
** Corresponding author*

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1. Introduction

Oral cancer is a major health concern, and it is considered the leading cause of death from oral disorders in numerous countries (Almangush et al., 2020). Squamous cell carcinoma (SCC) represents the most prevalent histological subtype of oral cancer, encompassing the majority of malignant lesions arising in the lip, oral cavity, and oropharynx. Oral Cavity Squamous Cell Carcinoma (OCSCC) is the most prevalent kind of cancer in Head and Neck Cancer (HNC). As a result of its metastatic nature and high recidivism rate, it is classified as one of the most aggressive malignant tumours (Chamoli et al., 2021). The carcinogenesis of SCC involves a complex interplay of genetic and epigenetic alterations that disrupt normal cellular regulatory mechanisms, ultimately driving the malignant transformation of oral mucosal epithelial cells (Szyfter, 2021).

Oral squamous cell carcinoma (OSCC) is mostly treated with surgical resection, either alone or in combination with adjuvant therapies such as radiotherapy or chemoradiotherapy (Huang & O'Sullivan, 2013; Ghanaati et al., 2025). The decision of using adjuvant treatment is governed by pathological risk factors found during the surgical specimen's standardised histological examination. These characteristics include tumour differentiation grade, invasion pattern, depth of invasion (DOI), margin status, perineural or lymphovascular invasion, and bone involvement (Rahadiani et al., 2022; Evans et al., 2025). Furthermore, nodal characteristics—such as the number of metastatic lymph nodes, the size of the biggest nodal metastasis, and the existence of extracapsular spread (ECS) or extranodal extension (ENE)—are important factors. Collectively, these measures guide postoperative pathological TNM (pTNM) staging and help with specific risk classification and treatment planning (Wreesmann et al., 2016). Metastasis to cervical lymph nodes develops in about 50% of individuals with oral cavity squamous cell carcinomas (SCC) and is a primary predictor of outcome in this illness (Patel & Lydiatt, 2008; Montero et al., 2014).

Tobacco consumption is a well-established aetiological factor in the development of OSCC. In addition to tobacco use, low socioeconomic status, limited access to healthcare, and a general lack of awareness or self-neglect are recognised as major contributing factors to OSCC incidence (Chamoli et al., 2021). The disease predominantly affects individuals over the age of 40, with a significantly lower incidence observed in younger populations. Epidemiological data further indicate a marked gender disparity, with a higher global incidence in males compared to females, estimated at 5.8 and 2.3 cases per 100,000 population, respectively (Chamoli et al., 2021).

Surgical intervention remains a cornerstone in the management of oral cancer, playing a vital role not only in tumour eradication but also in preserving the patient's quality of life. However, such procedures frequently result in significant anatomical and functional changes, potentially affecting speech, swallowing, and overall oral function. Consequently, postoperative rehabilitation is essential to support patients in regaining their ability to eat, speak, and engage socially (Gokavarapu et al., 2015).

Tumour resection may involve partial or total removal of critical structures such as the tongue, mandible, or adjacent soft tissues. These interventions can lead to impairments in articulation, deglutition, and oral hygiene maintenance. Additionally, psychological challenges—including anxiety and depression—may emerge due to alterations in physical appearance and diminished functional capacity, further complicating the recovery process. Therefore, a comprehensive rehabilitation approach addressing linguistic, physical, and psychological challenges is essential for optimal recovery following oral cancer surgery (Sharma et al., 2024).

An effective rehabilitation strategy requires the coordinated efforts of a multidisciplinary team of healthcare professionals, typically including speech-language pathologists, dietitians, physical therapists, psychologists, oral and maxillofacial surgeons, and dentists. Collaborative interdisciplinary care ensures the development of an individualised treatment plan that holistically addresses the patient's diverse needs. Rehabilitation programmes should be tailored to the specific type and extent of the surgical procedure, as well as to the patient's unique clinical condition and personal preferences (Taberna et al., 2020; Passchier et al., 2024).

Malignancies of the mandible, most commonly squamous cell carcinomas of the oral cavity, pose a distinctive clinical challenge due to their anatomical position, the likelihood of perineural invasion, and the disruption of maxillofacial integrity. Owing to their proximity to branches of the trigeminal and facial nerves, these tumours frequently result in neuropathic complications such as facial numbness, tingling sensations, or severe orofacial pain. The phenomenon of perineural invasion, often identified in histopathological assessment of advanced mandibular tumours, is not only a marker of aggressive disease but also a predictor of higher recurrence rates and less favourable prognosis, which underlines its neurological significance (Batsakis, 1985).

The neurological sequelae of mandibular cancer extend beyond sensory disturbances. When nerves such as the inferior alveolar or lingual are infiltrated or surgically compromised, patients frequently develop impairments in chewing, swallowing, and speech articulation. These motor deficits substantially reduce daily functional capacity and quality of life. Additionally, iatrogenic nerve damage during ablative procedures may intensify neuropathic pain or lead to persistent disability. Such consequences emphasise the importance of nerve-sparing surgical techniques and the integration of specialised neurorehabilitation into treatment plans (Liebig et al., 2009).

The psychological dimension of mandibular cancers is equally profound. As the mandible is essential for facial symmetry and expression, its surgical alteration or removal often leads to visible disfigurement. These aesthetic and functional changes frequently result in disturbances of body image, diminished self-confidence, and tendencies towards social withdrawal. Evidence consistently demonstrates that individuals treated for head and neck cancers experience disproportionately high levels of depression and anxiety compared to other oncology populations, largely due to their altered facial appearance and difficulties with speech (Dropkin, 1999).

Communication difficulties further amplify the psychological burden. Surgical removal or reconstruction of the mandible frequently interferes with speech clarity, leaving patients vulnerable to feelings of isolation, frustration, and stigmatisation in social interactions. Even when prosthetic rehabilitation or reconstructive surgery is successful, residual functional limitations often persist, undermining effective communication and exacerbating emotional distress (Rogers et al., 2008).

Another important consideration is the interaction between chronic neuropathic pain and mental health. Persistent pain symptoms can lead to secondary sleep disorders, fatigue, and cognitive strain, all of which exacerbate emotional disturbances such as anxiety and depression. This reciprocal relationship between somatic and psychological suffering underscores the necessity of a multidisciplinary approach. Optimal care for patients with mandibular cancers should integrate oncological treatment with structured psychological support, targeted pain management, and social rehabilitation programmes. Studies suggest that such comprehensive psycho-oncological care has a substantial impact on improving patients' functional outcomes and overall well-being (Hammerlid & Bjordal, 2001).

2. The Role of Artificial Intelligence in the Histopathological and Imaging Diagnosis of Oral Squamous Cell Carcinoma

2.1. Multi-Method Analysis of Histopathological Image for Early Diagnosis of Oral Squamous Cell Carcinoma Using Deep Learning and Hybrid Techniques

The aim of this study was to overcome the difficulties encountered by CNN-type models in the process of identifying histological images, with the intention of obtaining superior results, an essential aspect for the early detection of oral squamous cell carcinoma (OSCC).

To achieve this objective, the images in the dataset were processed and optimised in order to eliminate noise and reduce both time and hardware resources requirements. The process was achieved by integrating deep learning methods with classical machine learning techniques. In this research, several methods were applied for diagnosing OSCC using histopathological images. In addition, a complex approach was proposed, combining features extracted by deep learning models

with traditional features related to colour, texture, and shape. The essential contributions of this work can be summarised as follows:

• Improving the quality of histological images of oral cancer by applying two different filters, in order to facilitate a more precise extraction of relevant features.

• Optimising the performance of CNN models by adjusting hyperparameters, in order to obtain a more precise classification and higher accuracy.

• Proposing a hybrid diagnostic method based on combining CNN models with the SVM algorithm, capable of efficiently identifying cancer cells from histological images.

• Reducing the dimensionality of the OSCC dataset using the PCA algorithm, to simplify the analysis process and avoid feature redundancy.

• Performing the diagnosis of histological images of OSCC cells using the SVM algorithm, with a mixed set of features — both those generated by CNN models and the traditional ones of color, texture and shape.

The initial stage of this study aimed to improve the quality of histological images from the OSCC dataset, as they presented artefacts that affected the accuracy of the analyses. To achieve the proposed goal, three distinct methodological directions were applied, based on five different models. In the first approach, the dataset was classified using deep learning networks, specifically the Xception, InceptionV3, InceptionResNetV2, NASNetLarge, and DenseNet201 models.

The second strategy involved a hybrid method, combining the advantages of deep learning algorithms with the efficiency of the SVM classifier for improved performance in image recognition. The third approach consisted of using the SVM algorithm as the main classification method, based on a set of hybrid features obtained by integrating the features generated by deep learning models with those extracted by the traditional HOG, GLCM, and LBP algorithms, as illustrated in Figure 1.

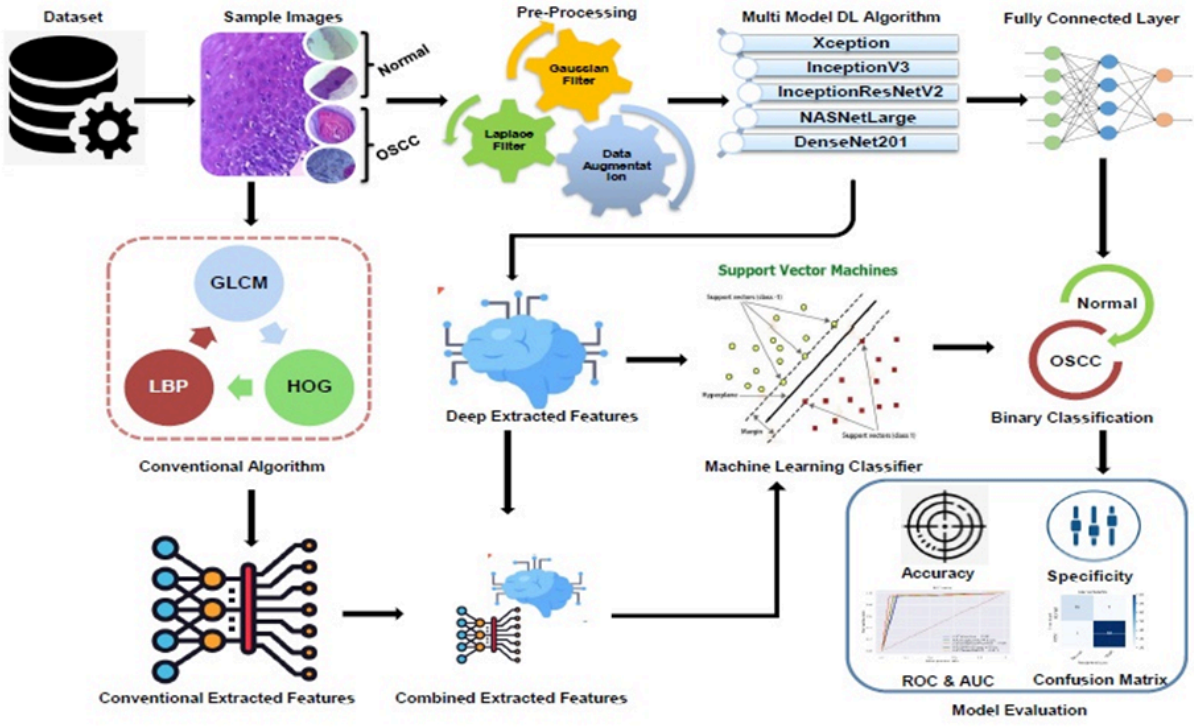

Figure 1. Proposed Method for Oral Squamous Cell Carcinoma (OSCC) Diagnosis
Source: Ahmad, M., Irfan, M. A., Sadique, U., Haq, I. U., Jan, A., Khattak, M. I., Ghadi, Y. Y., & Aljuaid, H. (2023). Multi-method analysis of histopathological image for early diagnosis of oral squamous cell carcinoma using deep learning and hybrid techniques. Cancers, 15(21), 5247. https://doi.org/10.3390/cancers15215247

The dataset used in this study included a total of 5192 histopathological images, obtained from biopsy sections photographed at 100× magnification. These images were collected from biopsies taken under local anaesthesia. The diagnosis of each sample was established by a pathologist. Of the 5192 images analysed, 2494 (48%) were labeled as normal tissues, and 2698 (52%) were identified as malignant oral squamous cell carcinoma (OSCC). The analysis performed in the study was based exclusively on these images.

The convolution layer is the fundamental element of a convolutional neural network (CNN), which is responsible for identifying and extracting relevant features from input data, such as images or audio signals. The operation of this layer is determined by three essential parameters: the step size (p-step), the zero padding, and the filter size. The filter size defines the number of pixels f(t) used to retrieve information from the input image x(t) through a "sliding window" mechanism. In order to maintain the original dimensions of the processed image, the zero padding technique was applied. The large number of parameters generated by convolutional layers can impose a considerable computational burden on convolutional neural networks (CNNs). To reduce this complexity, pooling layers have been introduced into the CNN architecture. Their role is to reduce the spatial dimension of the feature maps obtained after the convolution process.

Two techniques are generally used to reduce the size of images: max pooling and average pooling. In the case of max pooling, a filtering window selects a group of pixels in the image; from these, the pixel with the highest value is chosen, and the entire region is subsequently represented only by that maximum value.

In contrast, the average pooling method selects a region of pixels using a filter of a predetermined size, calculates the average of the values in that region, and replaces all pixels in the respective window with this average value, representative of the analysed area.

A dense layer, also called a fully connected layer (FCL), is a central element in the structure of artificial neural networks. Its main function is to transform multidimensional information from previous layers into a linear representation, easy to interpret by the output layer. Within a fully connected layer, each neuron is connected to all neurons in the previous layer, receiving from them signals weighted by a set of weights learned during the training process. These values are then processed by an activation function, which determines the final output of the neuron.

In the final phase, the layer employing the sigmoid activation function has the role of classifying the image, by analysing the degree of similarity with the different available classes. This function generates a probability value between 0 and 1, indicating the membership of the image to a certain class. In addition to the sigmoid, there are other commonly used activation functions, such as ReLU (Rectified Linear Unit), which leaves positive values unchanged, but transforms all negative values to zero, according to the corresponding formula.

In this section, an innovative method combining Convolutional Neural Networks (CNN) with the Support Vector Machine (SVM) algorithm is proposed. The core concept of this approach is to develop a hybrid solution capable of mitigating the limitations of traditional CNN models, in particular the high consumption of computing resources and the low processing speed.

The proposed hybrid method aims to provide a computationally efficient alternative that requires minimal hardware resources and enables rapid training on the dataset, thus leading to accurate and high-performance diagnostic results.

This hybrid strategy consists of two essential steps. In the first step, the histological images of OSCC are processed to improve their quality, after which the extraction of deep feature maps is performed using several CNN models, such as Xception, InceptionV3, InceptionResNetV2, NASNetLarge, and DenseNet201. The resulting features are stored in a feature vector and then passed to the SVM algorithm for classification.

In this architecture, the feature maps obtained from CNN models serve as input to the SVM, which replaces the final layers of the convolutional network. The SVM algorithm performs the final classification, providing an accurate diagnosis by analysing each extracted feature vector.

The feature extraction process is conducted across multiple layers and levels, each with the ability to identify unique types of features. In this study, deep information was obtained from the histological images of OSCC by using advanced neural network models, such as Xception, InceptionV3, InceptionResNetV2, NASNetLarge, and DenseNet201. The extracted features were then organised as feature vectors and passed to the machine learning (ML) model, which was responsible for the final image classification.

The Support Vector Machine model was used to replace the final layers of the CNN network. In the first stage, histopathological images were pre-processed by reducing noise and enhancing contrast in the region of interest. After optimisation, these images were used as input for the Xception, InceptionV3, InceptionResNetV2, NASNetLarge, and DenseNet201 models.

In the second stage, various models were used to extract features, which were then saved as feature vectors of size (n × m), where n denotes the number of samples and m corresponds to the number of feature vectors. In the final stage, the dimensionally reduced features were used by the SVM algorithm to perform classification, determining whether the image is normal or indicates the presence of OSCC.

The results indicated that the NASNetLarge model achieved remarkable performance, recording an accuracy of 94.44%, a specificity of 95.80%, a precision of 90.32%, a sensitivity of 87.52%, and an F1 score of 88.88%.

In turn, the DenseNet201 model stood out with an accuracy of 96.77%, a specificity of 98.87%, and an area under the ROC curve (AUC) of 94.70%.

The Xception model proved effective in analysing histopathological images used for OSCC diagnosis, achieving an overall accuracy of 90.47% and a cancerous image identification rate of 90.52%.

The InceptionV3 model stood out for its high performance in analysing histopathological images used for OSCC diagnosis, achieving an overall accuracy of 91.26% and a cancerous image detection rate of 92.63%.

The InceptionResNetV2 model stood out for its superior performance, achieving an overall accuracy of 92.85% and a cancer image recognition rate of 94.73% (Ahmad et al., 2023).

2.2. Accurate Real-Time Diagnosis of Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma Using Convolutional Neural Networks and High-Resolution In Vivo Confocal Microscopy

The study presents a total of fifty-nine patients who presented to the Department of Oral Medicine at the Royal Melbourne Dental Hospital (Melbourne, Australia) for the evaluation of oral mucosal abnormalities. They were investigated between 8 December 2020 and 13 March 2022 using the in vivo endomicroscope. For topical contrast imagining, fluorescein 0.1% and acriflavine 0.1% were utilised. In total, 9,168 images were obtained from different regions of the oral cavity, including the tongue, buccal mucosa, gingiva and vestibule, soft palate, hard palate, and floor of the mouth. After clinical assessment by an oral medicine specialist, patients underwent excision biopsy with a scalpel, followed by histopathological diagnosis. The biopsy site was selected by the attending physician prior to performing confocal imaging.

The InVivage confocal microscope offers a lateral resolution of 0.55 μm and an axial resolution of 5.1 μm, with a field of view of 475 × 475 μm and a z-axis depth of focus of 400 μm. During image acquisition, the scan plane was positioned parallel to the tissue surface and the z-axis was oriented perpendicular to it, following the depth of the tissue, as illustrated in Figure 1A, B, and C. An NVIDIA RTX 3050 graphics card was used to train and test the convolutional neural networks (CNN) used in image analysis, along with an AMD Ryzen 5000 series processor and 16 GB of RAM. In this study, the term “images” refers to the individual frames (or sections) obtained by the in vivo confocal microscope along the z-axis, during the recording of a sequential set of images, as illustrated in Figure 1B and C.

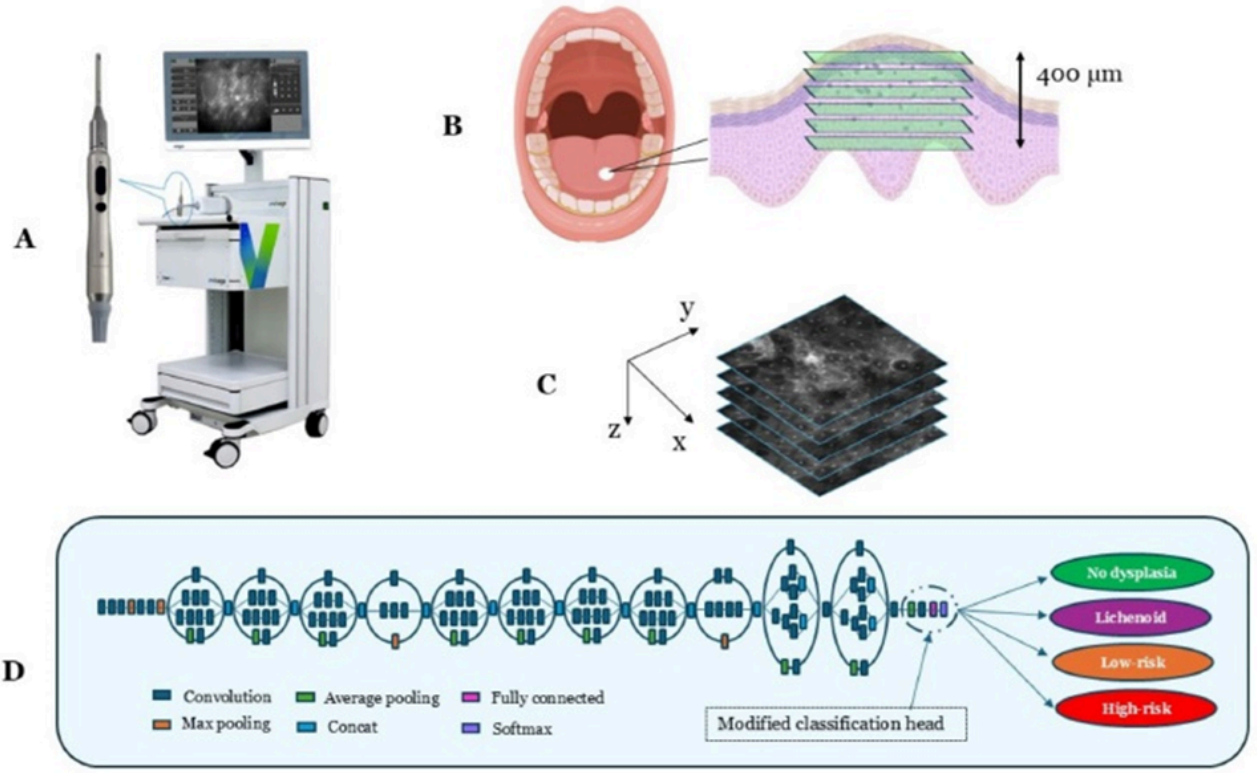

Figure 2. In vivo confocal microscopy image acquisition and CNN architecture: (A) The InVivage confocal endomicroscope equipped with a handheld probe (inset);(B) En face image stacks acquired to a maximum depth of 400 µm within the oral epithelium;(C) Schematic representation of an image stack captured along the z-axis;(D) The modified Inception_v3 convolutional neural network architecture employed for the PMAC diagnostic models. Source: Ramani, R. S., Tan, I., Bussau, L., O'Reilly, L. A., Silke, J., Angel, C., Celentano, A., Whitehead, L., McCullough, M., & Yap, T. (2025). Convolutional neural networks for accurate real-time diagnosis of oral epithelial dysplasia and oral squamous cell carcinoma using high-resolution in vivo confocal microscopy. Scientific Reports, 15, 2555. https://doi.org/10.1038/s41598-025-86400-5

The convolutional neural network (CNN) architecture applied in this study was based on a modified Inception_v3 model, in which the final classification layer was replaced by a new fully connected layer designed for classifying the specific categories analysed, using the transfer learning technique. Before importing the images into the PyTorch development environment, they were subjected to preprocessing steps, which included converting the format from DICOM to TIFF and resizing from 1024 × 1024 to 299 × 299 pixels, according to the input requirements of the Inception_v3 model. These operations were performed using the open-source image analysis software Fiji (ImageJ).

In the study, three distinct types of convolutional neural networks (CNNs) were developed, designed to perform two main functions: image quality filtering and diagnostic sorting, applied to images obtained with the two contrast agents — acriflavine and fluorescein.

The dedicated image quality filtering model, called Quality Micrograph Refiner (QMR), was implemented for both types of agents and constituted the preliminary stage before the application of specialised diagnostic sorting models. These specific models were called the Fluorescein Pathologic Micrograph Allocation CNN (FPMAC), for images obtained with fluorescein, and the Acriflavine Pathologic Micrograph Allocation CNN (APMAC), for those obtained with acriflavine.

In total, 270 CNN models were created, trained, and evaluated, corresponding to different combinations of number of epochs, learning rates, and cross-validation folds for both contrast agents, all of which were implemented in the PyTorch environment.

2.2.1. QMR CNN Model Performance Results

Analysis of the CNN network performance on the test dataset indicated that the most efficient combination of hyperparameters was obtained at 15 epochs and a learning rate of 0.01. The average of the performance metrics corresponding to this configuration, calculated over the five cross-validation folds, showed an overall accuracy of 88.1%, with a sensitivity of 0.78, specificity of 0.94, precision of 0.90, and an F1 score of 0.83. The individual model that achieved the highest performance score for the optimal combination of hyperparameters was selected as the final QMR model. It demonstrated an accuracy of 89.5%, with a sensitivity of 0.81, specificity of 0.95, precision of 0.91, and an F1 score of 0.86, requiring only 0.03 seconds to analyse each image.

2.2.2.Training and Testing the Acriflavine PMAC (APMAC) Model

Among the 90 APMAC models developed and evaluated for the different diagnostic categories (no dysplasia, lichenoid lesions, low risk, and high risk), the best performing combination of hyperparameters—having the best overall values for sensitivity, specificity, accuracy, and F1 score—was obtained at 30 epochs and a learning rate of 0.001. This configuration was therefore adopted as the final APMAC model.Within this model, F1 scores were high for lichenoid lesions (0.78) and low risk (0.82), while for the no dysplasia and high risk categories, F1 score values were much lower, at 0.05. The best performances of the APMAC model were recorded for the floor of the oral cavity (F1 score = 0.83) and the oral mucosa (F1 score = 0.77), while the worst results were observed for the hard palate (0) and gingiva and vestibule (0.17).

2.2.3.Training and Testing the Fluorescein PMAC (FPMAC) Model

Among the 90 FPMAC models developed and evaluated for all diagnostic categories (no dysplasia, lichenoid lesions, low risk, and high risk), the most efficient combination of hyperparameters, which obtained the best values for sensitivity, specificity, accuracy, and F1 score, was the one corresponding to a 25-epo training with a learning rate of 0.001. This configuration was designated as the final FPMAC model.

The model obtained the highest F1 scores for the lichenoid (0.86) and low risk (0.83) classes, while for no dysplasia and high risk, the F1 score values were 0.76 and 0.78, respectively. The best performances of the FPMAC model were recorded for the soft palate (F1 = 1) and the floor of the mouth (F1 = 0.93), while the lowest scores were observed for the tongue (F1 = 0.62), gingiva and vestibule (F1 = 0.76). The AUC values obtained for the ROC curves related to the classes without dysplasia (AUC = 0.91), lichenoid (AUC = 0.96), low risk (AUC = 0.90), and high risk (AUC = 0.96) highlight the high ability of the model to correctly differentiate between lesion types.

The convolutional neural network (CNN) models developed in this study convincingly demonstrate the potential to achieve accurate diagnostic triage of oral mucosal diseases, in a manner comparable to the histopathological diagnosis used in routine clinical practice. Implementation of this technology could significantly reduce the need for surgical biopsies, by correctly detecting the majority of dysplastic lesions of the oral epithelium (Ramani et al., 2025).

2.3. Oral Squamous Cell Carcinoma Diagnosis in Digitised Histological Images Using Convolutional Neural Network

The aim of this study was to develop an artificial intelligence system capable of identifying both cellular and structural atypia to diagnose the full spectrum of squamous cell carcinoma (SCC), including well-differentiated forms with apparently normal cytology. To achieve this goal, the training datasets included extended images (large fragments) at different magnification levels,

mimicking the way a pathologist examines specimens for diagnosis. Samples were collected by biopsy or surgery from 90 patients, randomly selected from those diagnosed with squamous cell carcinoma (SCC) between 2018 and 2020, at a university dental hospital.

The image fragments were divided into four categories: “cancer”, “non-cancer”, “suspect”, and “unknown”. Any image that showed even a very small amount of cancerous tissue was classified as “cancer”, while images that contained only normal structures, such as muscle, connective tissue, minor salivary glands, or granulation tissue, were classified as “non-cancer”.

EfficientNet is a high-performance image classification model based on convolutional neural networks (CNNs) that has achieved top-notch results on the ImageNet dataset. It offers superior accuracy and efficiency compared to previously established convolutional networks, such as ResNet, DenseNet, Inception, and Xception. Given that the number of parameters and computational complexity increase exponentially with the size of the EfficientNet architecture, the simplest variant, EfficientNet B0, was chosen for the classification model. Its parameters were initialised with weights pre-trained on the ImageNet dataset. As the ImageNet model weights were not trained on histopathological images, neither replacing fully connected layers nor blocking any layers was recommended. Consequently, the fine-tuning process was applied to all layers of the EfficientNet B0 model.

Grad-CAM analysis showed that the AI focused on relevant cancer features in the assessment process. Thus, in high-magnification images of tumour tissue, the AI highlighted keratin pearls and ectopic keratinisation—characteristic signs of well-differentiated squamous cell carcinoma (SCC). In cases of moderately differentiated and poorly differentiated SCC, the AI adequately focused on invasive tumour nests and atypical cells. In low-magnification images (approximately 5×), the AI’s attention was directed to abnormal structures, such as irregular growth of epithelial components, atypical distribution of stromal tissue, and ectopic keratinisation.

A tendency for the AI to focus on the area around the basal layer was also observed. In high-magnification images of tumour tissue—particularly when the lesion showed lamellar proliferation and lacked obvious keratinised nests—the AI focused on the outer edges of the cancerous parenchyma. In images without cancerous lesions, the AI’s attention was drawn to the transition zone between the epithelium and the juxtaepithelial stroma, regardless of the magnification. When the image captured all layers of the stratified squamous epithelium at high magnification, the focus was distributed relatively evenly throughout the thickness of the epithelium.

However, some misclassification errors were identified, including both false positives and false negatives. For example, the AI failed to detect a cancerous portion located in a corner of the image, likely due to excessive focus on the unlesioned region. Additionally, in a few cases, structures such as minor salivary glands, muscle fibres, or blood vessels located at the periphery of the image fragments were erroneously interpreted as cancerous tissue, as illustrated in Figure 3.

The trained AI model demonstrated high classification performance. It reacted very little to structures that do not belong to stratified squamous epithelium — such as granulation tissue, altered muscle fibres, or endothelial cells with enlarged nuclei — which can easily mislead an inexperienced observer. Thus, the AI seems to have learned the characteristic features of squamous cell carcinoma (SCC). At high magnification, tumour images showed clear signs of cancerous cellular atypia, such as enlarged nuclei, anisokaryosis, increased nuclear-to-cytoplasmic ratio, nuclear hyperchromatism, and large nucleoli. In low-magnification images (approximately 5×), the AI was able to identify cancerous components even in the absence of well-defined cellular morphology.

The model adequately focused on signs of structural atypia — such as irregular growth of epithelial components, ectopic keratinisation, and abnormal stromal distribution caused by unusual hyperplasia of stratified squamous epithelium — to classify the lesion image as cancer. These results indicate that AI is able to distinguish cancerous from normal tissue based on structural atypia, even in the absence of precise details about cellular atypia. Overall, the findings support

that, through the proposed method, AI was able to learn the characteristics of both cellular and structural atypia specific to squamous cell carcinoma (SCC) (Oya et al., 2023).

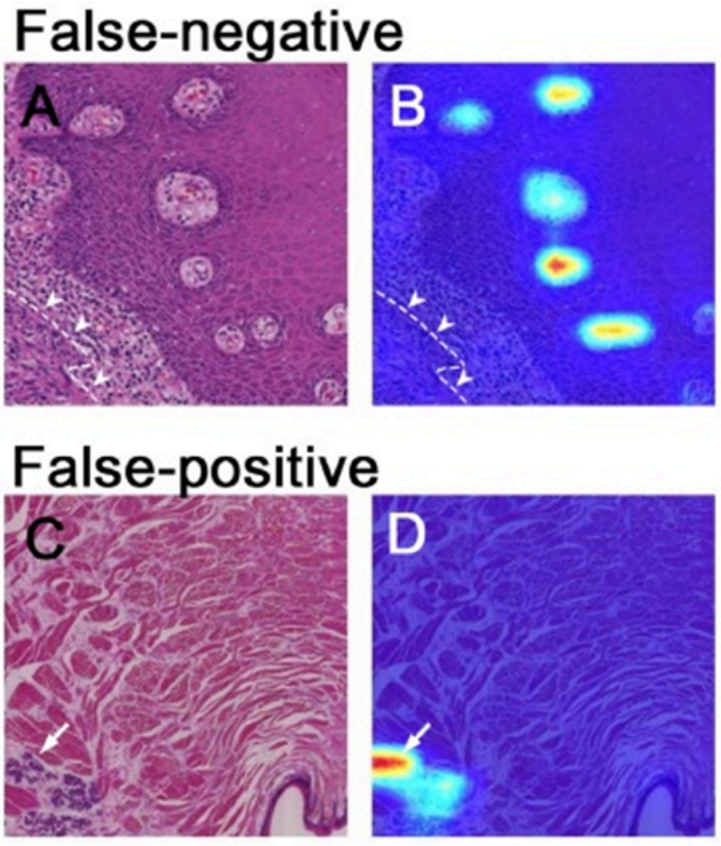

Figure 3. Examples of false negatives (A, B) and false positives (C, D). The artificial intelligence (AI) did not identify the tumour component located in the corner of the image (A, B, arrow), focusing instead on the normal interstitial tissue (B). In some cases, minor salivary glands located at the periphery of the images (C, arrow) were misinterpreted as cancerous formations (D, arrow). Source: Oya, K., Kokomoto, K., Nozaki, K., & Toyosawa, S. (2023). Oral squamous cell carcinoma diagnosis in digitized histological images using convolutional neural network. Journal of Dental Sciences, 18(1), 322–329. https://doi.org/10.1016/j.jds.2022.08.017

2.4. Application of CT and MRI Images Based on Artificial Intelligence to Predict Lymph Node Metastases in Patients with Oral Squamous Cell Carcinoma

Recently, artificial intelligence (AI) has been increasingly used in radiological image analysis, due to its ability to automatically identify complex patterns in imaging data and provide objective quantitative analyses, as opposed to purely qualitative assessments traditionally performed by specialists. Today, AI systems based on radiological features have become a valuable tool in the field of oncology, contributing to the diagnosis and staging of tumours, as well as to the estimation of therapeutic response and patient prognosis. Through these applications, AI confirms its potential to become a complementary, non-invasive tool in support of personalised medicine.

In recent years, several studies have explored the use of machine learning (ML) and deep learning (DL) algorithms to predict lymph node metastases in patients diagnosed with oral squamous cell carcinoma (OSCC), obtaining encouraging results in terms of model accuracy and performance. The studies analysed were published between 2019 and 2023 and were entirely retrospective in nature. Geographically, the majority of the research—seven papers—was conducted in China, while five originated from Japan and two from Italy. Regarding the types of artificial intelligence algorithms used, five studies applied deep learning (DL) methods, and ten studies used

machine learning (ML) algorithms. One of these studies combined the two approaches, separately analysing the effectiveness of a hybrid (fusion) model.

Regarding the radiomic features analysed, five studies extracted tumour or lymph node characteristics from MRI images, while nine derived this information from CT images. Only two studies implemented an automated extraction of radiomic features, the rest relying on manual processing, performed by specialised and experienced radiologists.

Additionally, seven of the included studies provided a direct comparison between the performance of artificial intelligence models and the diagnostic accuracy of experienced radiologists, to evaluate the potential of AI as a support tool in the interpretation of medical images. Cumulative analysis of the results showed that the machine learning (ML) models used for the prediction of lymph node metastases achieved high performance, with the following mean values: AUC of 0.91 (95% confidence interval: 0.88–0.93), sensitivity of 0.84 (95% CI: 0.74–0.90), and specificity of 0.87 (95% CI: 0.82–0.90). These results highlight the robust ability of ML algorithms to differentiate patients with lymph node metastases from those without, confirming the high potential of artificial intelligence in the diagnosis and staging of oral squamous cell carcinoma (OSCC).

Integrated data analysis revealed that the Deep Learning (DL) models used to estimate the risk of nodal metastases showed a high overall performance, characterised by the following mean values: AUC of 0.92 (95% confidence interval: 0.89–0.94), sensitivity of 0.74 (95% CI: 0.44–0.91), and specificity of 0.90 (95% CI: 0.81–0.95). Based on these results, it can be concluded that both machine learning (ML) and deep learning (DL) models have a solid ability to predict the presence of nodal metastases. The comparative analysis did not reveal statistically significant differences between the performances of the two types of algorithms, suggesting that both approaches may be effective in this clinical context. In the subgroup analysis, performed according to the imaging modality used, notable differences were observed between CT-based and MRI-based models:

In nine studies, AI models were trained using features extracted from CT images, achieving high performance, with aggregate values of: AUC = 0.94 (95% confidence interval: 0.92–0.96), sensitivity = 0.81 (95% CI: 0.62–0.92), and specificity = 0.92 (95% CI: 0.87–0.95).

In contrast, five studies used magnetic resonance imaging (MRI) to train AI algorithms, reporting more modest pooled values: AUC = 0.89 (95% CI: 0.86–0.91), sensitivity = 0.84 (95% CI: 0.69–0.93), and specificity = 0.84 (95% CI: 0.77–0.90). The overall analysis suggests that CT-derived AI models provide superior accuracy in identifying nodal metastases in patients with oral squamous cell carcinoma (OSCC). By comparison, MRI-based models showed significantly lower performance, especially in terms of combined AUC, indicating a lower efficiency of this imaging modality for predicting nodal metastases in OSCC.

Six studies that provided sufficient comparative information evaluated the differences in diagnostic performance between artificial intelligence (AI) models and experienced radiologists. For AI models applied to predict lymph node (LN) metastases, the cumulative performance was high, with the following values: AUC = 0.93 (95% confidence interval: 0.90–0.95), sensitivity = 0.83 (95% CI: 0.73–0.90), and specificity = 0.90 (95% CI: 0.82–0.95). By contrast, experienced radiologists recorded slightly lower values: AUC = 0.81 (95% CI: 0.78–0.85), sensitivity = 0.73 (95% CI: 0.65–0.79), specificity = 0.90 (95% CI: 0.83–0.95). The overall analysis shows that, although imaging specialists demonstrated appreciable ability to recognise nodal metastases, AI-based models achieved superior results in terms of overall accuracy (AUC). This finding highlights the significant potential of AI to become a valuable complementary tool in the imaging evaluation of patients with oral squamous cell carcinoma (OSCC).

In recent years, artificial intelligence (AI) technologies applied to medical imaging have developed rapidly and have begun to be integrated into clinical practice. Based on the analysis of large volumes of data and deep learning algorithms, AI has the ability to automatically identify complex features in medical images, providing their accurate and consistent interpretation. One of the important branches of this direction is radiomics — a method that uses manually extracted

features from images, allowing for their detailed quantitative analysis. The information obtained is then used as input for machine learning (ML) models, which are trained to classify patients and support the clinical decision-making process through objective and reproducible estimates. On the other hand, deep learning (DL) represents a different and more advanced approach, capable of automatically extracting high-level features directly from images, without human intervention. This method preserves data fidelity and objectivity, and has demonstrated exceptional performance in a variety of medical applications.

Compared to conventional diagnostic methods, AI-based models offer significant advantages, such as reproducibility of results, elimination of subjectivity, and rapidity in obtaining interpretations.Currently, ML and DL models derived from medical imaging are being intensively researched for the assessment of lymph node (LN) status and have demonstrated promising potential in improving the accuracy and efficiency of diagnostics in head and neck oncology, including oral squamous cell carcinoma (OSCC) (Deng et al., 2024).

2.5. Prediction of Bone Invasion of Oral Squamous Cell Carcinoma Using a Magnetic Resonance Imaging-Based Machine Learning Model

The aim of this study is to develop a machine learning (ML) model that uses radiomic analysis of magnetic resonance images (MRI) to identify oral squamous cell carcinoma (OSCC) and estimate the risk of bone metastasis. The study included 86 patients — 42 women and 45 men — aged between 45 and 74 years, with an average age of 58.3 years.

MRI images were analysed for each participant and then classified into two categories: 44 benign cases, with no signs of bone invasion, and 42 malignant cases, with bone invasion. Radiomics is an innovative field of medical imaging that allows the transformation of image data into an extensive set of quantifiable features, through a large number of automated algorithms specialised in feature extraction and analysis. In this study, the Radcloud platform (Huiying Medical Technology Co., Ltd., Beijing, China) was used to collect and manage imaging and clinical data, as well as to perform radiomic statistical analyses. Such platforms dedicated to radiomics offer the possibility of identifying specific imaging patterns and signatures that can accurately reflect the state of a disease, thus contributing to obtaining essential information for the application of personalised medicine.

Using the Radiomics platform, 247 radiomic features were extracted from the volumes of interest (VOIs) of MRI images. These features were grouped into three broad categories: first-order features, which describe the distribution of signal intensity; shape features, which reflect the geometry of the lesion; and texture features, which capture the internal structural variations of the analysed tissue.

All statistical analyses were performed using the Radcloud platform (Huiying Medical Technology Co., Ltd., Beijing, China). A random number generator was used to divide the data, with 80% of the volumes of interest (VOIs) being allocated to the training set and 20% to the validation set, thus ensuring a balanced distribution of the data. In order to build models capable of predicting bone invasion, six classification algorithms were tested: Logistic Regression (LR), Random Forest (RF), Decision Tree (DT), k-Nearest Neighbors (KNN), XGBoost, and Support Vector Machine (SVM). These classifiers were used to identify the model with the highest performance in estimating the risk of bone invasion based on radiomic features extracted from MRI images.

The SVM (Support Vector Machine) algorithm emerged as the best performing classifier in both the training and testing sets, achieving superior diagnostic accuracy as confirmed by the analysis of four main evaluation parameters. Regarding the selection of radiomic features, the SVM method recorded remarkably high area under the curve (AUC) values — 0.999 for the training set and 0.934 for the validation set, confirming the excellent discrimination capacity of the model in predicting bone invasion. In contrast to other previously published research, this study applied six machine learning (ML) algorithms: neural networks (NN), support vector machine (SVM),

XGBoost, random forest (RF), logistic regression (LR), and decision tree (DT). Among all the algorithms tested, the SVM model stood out for its highest overall performance, obtaining the best values for area under the curve (AUC), precision, sensitivity, specificity, F1 score, as well as for the accuracy and recall indicators, confirming the superior efficiency of this method in radiomic analysis (Öztürk et al., 2024).

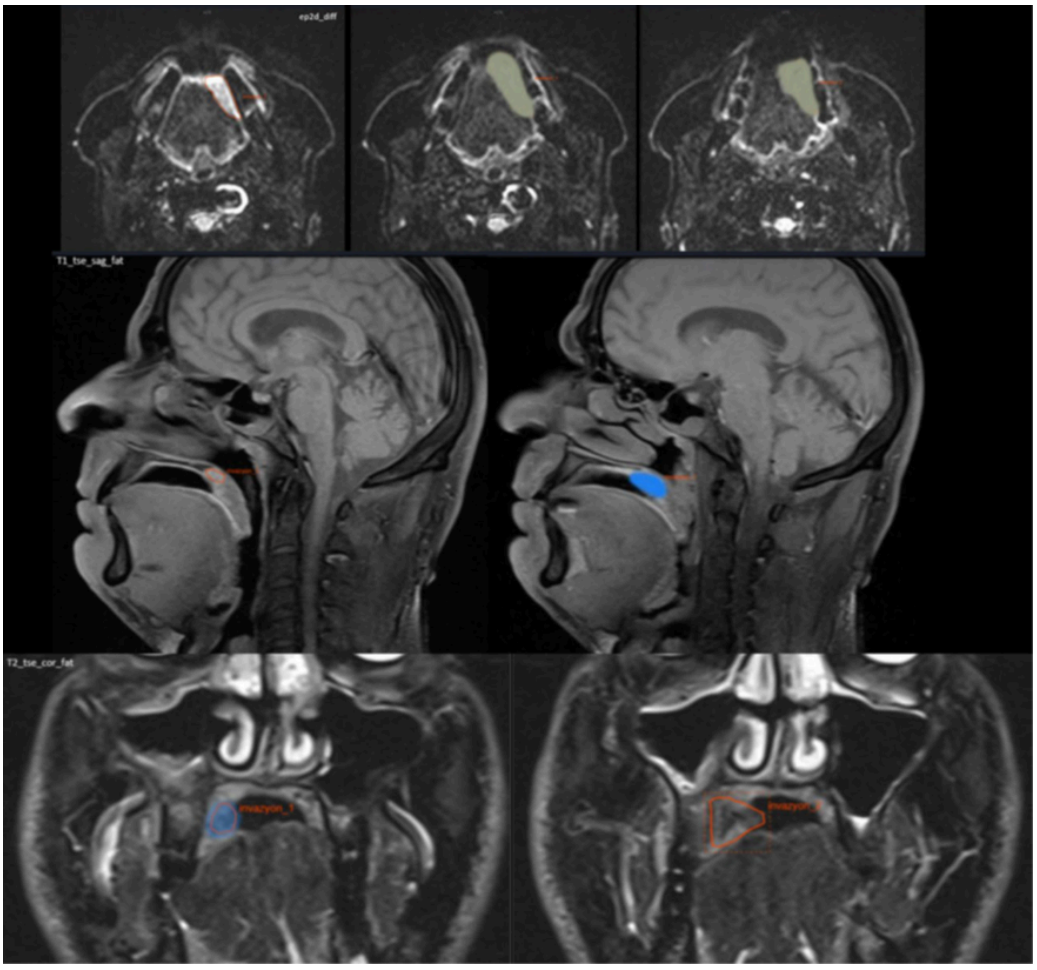

*Figure 4. MRI images illustrating **bone invasion segmentation** performed using the **SVM machine learning model**, showing a comparison between **manual segmentation** and **AI-based segmentation** across **axial**, **sagittal**, and **coronal** planes on various MRI sequences.Source: Öztürk, E. M. A., Ünsal, G., Erişir, F., & Orhan, K. (2024). Prediction of bone invasion of oral squamous cell carcinoma using a magnetic resonance imaging-based machine learning model. European Archives of Oto-Rhino-Laryngology, 281(12), 6585–6597. https://doi.org/10.1007/s00405-024-08862-z*

2.6. Value of PET Radiomic Features for Diagnosis and Reccurence Prediction of Newly Diagnosed Oral Squamous Cell Carcinoma

In patients with newly diagnosed oral squamous cell carcinoma (OSCC), accurate tumour staging from the initial stage is crucial to allow for a correct diagnosis, the selection of an appropriate therapeutic strategy, and the estimation of an individualised prognosis. The classification process is based on the assessment of the size and extent of the primary tumour (T stage), the involvement of regional lymph nodes (N stage), and the presence of distant metastases (M stage). The presence of metastases in the cervical lymph nodes is one of the most significant factors of unfavourable prognosis. Although distant metastases occur rarely, they are generally considered untreatable, necessitating adaptation and modification of the treatment plan.

Tumour grade reflects the level of differentiation of the neoplastic tissue, and constitutes an important indicator of the biological behaviour of the tumour. In general, a tumour with a

heterogeneous structure suggests a more advanced tumour grade and a more aggressive biological potential. This heterogeneity, along with other morphological and functional features of the tumour, can be identified through radiomic analysis. Radiomic features are obtained from the segmented tumour and describe in detail the shape, intensity distribution, and internal texture of the lesion. Accordingly, these radiomic features can provide valuable additional information that contributes to the precision of the diagnosis and the estimation of the prognosis in patients with oral squamous cell carcinoma (OSCC).

This study investigates whether radiomic features extracted from PET images of patients newly diagnosed with oral squamous cell carcinoma (OSCC), who have not yet received treatment, can be used to predict: (a) primary tumour stage, (b) histological grade of the tumour, (c) lymph node involvement, and (d) probability of recurrence. Only radiomic features that were shown to be: (a) constant across different segmentation methods and (b) independent of parameters such as tumour volume, maximum uptake value (SUVmax), and mean uptake value (SUVmean) were considered in the analysis.

To interpret the decisions generated by the prediction model, SHAP (SHapley Additive exPlanations) values were analysed, which provide a detailed understanding of the contribution of each radiomic feature to the final model results. The following study presents additional analyses derived from a previously published prospective study. A total of 138 patients with clinically suspected oral squamous cell carcinoma (OSCC) were prospectively enrolled between June 1, 2013, and January 31, 2016. Before any additional invasive procedures—such as panendoscopy or biopsy—were performed, all patients underwent a whole-body [18F]FDG PET/CT scan.

Surgical excision of the tumour was performed within two weeks of the imaging examination. The harvested tissues, specifically the primary tumour and lymph nodes, were analysed histopathologically; this evaluation represents the reference standard for determining tumour stage (T-stage), histological grade, and metastatic nodal involvement. All patients included in the analysis were previously untreated, and had not undergone any treatment prior to inclusion in the study.

A total of 445 radiomic features were extracted and analysed from the segmented volumes of interest (VOIs) using the RaCaT programme (version v.1.2733), developed in accordance with the standards established by the Image Biomarker Standardization Initiative (IBSI). To ensure uniformity of the imaging data, the images were resampled to isotropic 2 mm voxels, applying the tri-linear interpolation method. A classification model based on the Random Forest algorithm was trained to fulfill four distinct classification objectives: to determine tumour stage (T-stage) by differentiating between early-stage and advanced-stage tumours; to assess tumour histological grade by separating low-grade from high-grade cases; to identify the presence or absence of lymph node metastases and to classify recurrences. To obtain the most accurate assessment of classification performance, a 10-fold cross-validation method was used.

Within each iteration, the dataset was randomly divided into two subsets: a training set, comprising 90% of the patients, and a test set, representing 10% of the total cases. To compensate for the imbalance between classes (the numerical difference between positive and negative cases), the SMOTE algorithm – Synthetic Minority Over-Sampling Technique, was applied, which artificially creates additional examples from the minority class, thereby improving the stability of the model.

Additionally, to verify the robustness of the results, the bootstrap method with replacement was used, whereby 95% of the training data were randomly selected to generate new sets of training samples. Other types of classification algorithms were also evaluated to determine their applicability in the proposed analysis. These included Support Vector Machine (SVM), AdaBoost, and a series of randomised decision trees. Since the performances obtained were comparable between all tested models, it was decided to use the Random Forest classifier as the main method in the present study. The optimisation of the hyperparameters of the Random Forest model was achieved by stratified splitting of the training set into two subsets: 80% for training and 20% for

validation. An individual search for the optimal set of hyperparameters was performed for each classification task (further details are available in the appendix).

The performance evaluation of the classification model was carried out by determining several statistical precision indicators, including overall accuracy, area under the ROC curve (AUC), positive predictive value (PPV), negative predictive value (NPV), true positive rate (TPR), false positive rate (FPR), F1 score, as well as the Matthews correlation coefficient (MCC), which was used to evaluate the overall balance of the classifier performance. The classifier demonstrated robust performance in predicting tumour stage (low versus high T-stage), achieving an average accuracy of 85% (standard deviation 15%) and an average area under the curve (AUC) of 0.82 (standard deviation 0.19; 95% confidence interval: [0.68–0.95]) in cross-validation.

Positive predictive value (PPV) and negative predictive value (NPV) indicators reached values of 91% (standard deviation 11%) and 81% (standard deviation 30%), respectively. Thus, the model has a 91% probability that a tumour classified as high stage is indeed high stage, and an 81% probability that a tumour identified as early stage is actually low stage. The average values obtained for the false positive rate (FPR) and true positive rate (TPR) were 25% (standard deviation 30%) and 90% (standard deviation 11%). Regarding the other performance indicators, the F1 score had an average value of 0.89 (standard deviation 0.07), and the Matthews correlation coefficient (MCC) reached an average value of 0.66 (standard deviation 0.23).

The analysis of the calibration curves demonstrates that the model is well calibrated. However, the high standard deviation (30%) for NPV and TPR suggests a considerable variation in performance between the different iterations of the cross-validation process. This fluctuation is most likely the result of the differences between the training and testing datasets used in each round. As shown by the SHAP dependence plots, some advanced tumours exhibit similar radiomic features, while others differ significantly. When feature values are comparable between the training and test sets, the true positive rate (TPR) tends to be higher. Conversely, if advanced tumours with similar features predominate in the training set and advanced tumours with distinct features appear in the test set, the TPR decreases.

Regarding the classification of histological grade of the tumour, the classification model achieved a mean accuracy of 55% (standard deviation of 13%) and a mean area under the ROC curve (AUC) of 0.56 (standard deviation of 18%; 95% confidence interval: [0.43–0.68]). The positive predictive value (PPV) was relatively high, reaching 75% (standard deviation of 15%), while the negative predictive value (NPV) was significantly lower, at 28%. In addition, the false positive rate (FPR) and true positive rate (TPR) had values of 48% and 56%, respectively. The F1 score had a mean value of 0.74 (standard deviation of 0.07), and the Matthews correlation coefficient (MCC) was 0.26 (standard deviation of 0.22), suggesting a slightly superior performance to chance. For tumour grade prediction, the most frequently selected radiomic features across iterations were “Large zone high grey level emphasis (GLSZM2Davg)” and “Zone size variance (GLSZM2Dvmrg)”, which were included in 4 and 3 validation rounds, respectively.

The fact that a considerable number of features were selected in only one iteration indicates the absence of a dominant radiomic feature with stable predictive value across the entire dataset.
In predicting lymph node involvement, the classification model achieved a mean accuracy of 67% (standard deviation 9%) and a mean area under the ROC curve (AUC) of 0.64 (standard deviation 0.11; 95% confidence interval: [0.56–0.71]).

The positive predictive value (PPV) of 82% (standard deviation 10%) indicates that in more than 8 out of 10 cases, the model’s prediction of lymph node metastasis was accurate, with patients actually having lymph node involvement. In contrast, the negative predictive value (NPV) was lower, at 53% (standard deviation 25%). At the same time, the false positive rate (FPR) had an average value of 42% (standard deviation 29%), and the true positive rate (TPR) was 70% (standard deviation 19%). The relatively large standard deviations—25% for NPV and 29% for FPR—highlight a considerable variability in performance between different cross-validation iterations. This variation is explained by the fact that none of the radiomic features analysed

consistently fails to predict lymph node involvement. Consequently, tumours with and without lymph node metastases may exhibit similar radiomic characteristics, making it difficult for the model to accurately differentiate between them.

In conclusion, this prospective study evaluates the role of radiomic features in newly diagnosed, treatment-naïve patients with oral squamous cell carcinoma (OSCC) analysed before tumour resection and cervical dissection. The results indicate that radiomic analysis has the potential to distinguish with satisfactory accuracy between early-stage and advanced (T-stage) tumours. However, the same features were not effective in differentiating tumour histological grade, identifying lymph node metastases, or predicting the risk of recurrence (Pfaehler et al., 2025).

3. Clinical and Histopathological Evaluation of Mandibular OSCC: Case-Based Observations

While artificial intelligence provides powerful tools for automated detection and classification of OSCC, clinical validation and histopathological understanding remain essential. The clinical and histopathological cases presented below illustrate the morphological complexity and diagnostic challenges of oral squamous cell carcinoma (OSCC), particularly when located in the mandibular region. Such variability in tissue architecture, keratinisation patterns, and cellular atypia often makes accurate diagnosis and grading dependent on the pathologist's expertise and subjective interpretation.

In this context, artificial intelligence–based diagnostic systems, trained on large datasets of histopathological and clinical images, hold promise for reducing interobserver variability and improving diagnostic precision. By recognising subtle texture and morphological features that may elude the human eye, AI algorithms can complement conventional pathology, assisting in lesion classification, margin assessment, and early detection.

Tumour lesion biopsies were collected from subjects who presented to the Oral and Maxillofacial Surgery Department of the Emergency County Hospital of Craiova between March 1, 2025, and July 20, 2025. Excisional biopsies were performed using the classical scalpel-based surgical technique, followed by thorough irrigation with antiseptic solutions and primary wound closure by suturing. For all subjects, a clinical observation file was completed, and informed consent was obtained for both the biopsy procedure and the photographic documentation of the lesion. The tumour lesions were located at the level of the mandibular ramus, as well as the mandibular body, frequently in the paramedian region.

Tissue specimens were fixed in 10% neutral buffered formalin for 48 hours to ensure optimal preservation of cellular architecture. Subsequent processing was performed in the Histology Laboratory of the University of Medicine and Pharmacy of Craiova. Standard histological procedures were followed: tissue blocks were embedded in paraffin, serial sections of 4 μm thickness were obtained using an automated rotary microtome, and stained with routine haematoxylin and eosin (H&E) for general histological evaluation. Prepared slides were mounted using Canada balsam and analysed under light microscopy.

In all examined cases, we observed significant osseous defects following tumour removal, which are likely toimpact the physiological maintenance of mastication and swallowing processes, progressively leading to disorders of the temporomandibular joint over time, as illustrated in Figure 5 and Figure 6. Additionally, in one subject, impairment of facial function was noted due to marked asymmetry, the tumoural lesion being of considerable size.

Microscopic examination revealed, in the case of mandibular carcinomas, the presence of numerous keratin pearls, while in mesenchymal tumours, a significant number of spindle-shaped, atypical cells with elongated and hyperchromatic nuclei were observed, as shown in Figure 7 and Figure 8.

3.1. Intraoperative Aspects

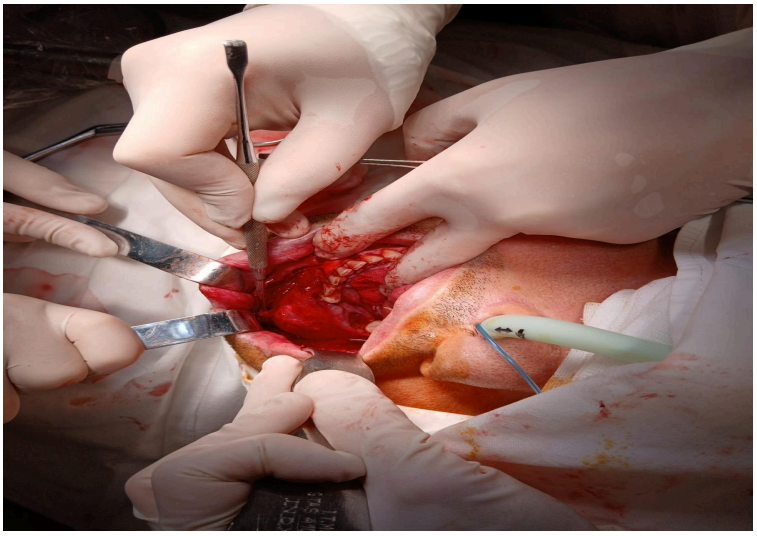

Figure 5. Mandibular squamous cell carcinoma – irregularly shaped tumour lesion located paramedianly on the horizontal branch of the mandible, measuring 6cm in diameter. The tumour caused mobility of the teeth within the lesion as well as adjacent teeth. Complete surgical excision of the lesion resulted in a significant bone defect.

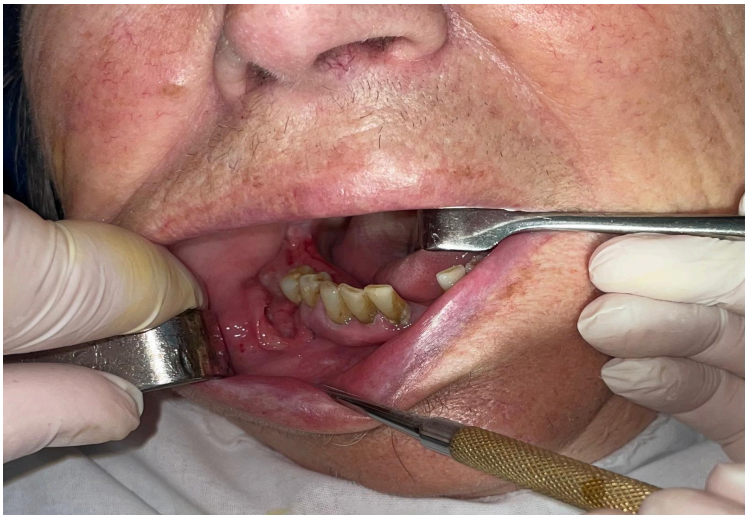

Figure 6. Mandibular squamous cell carcinoma – irregularly shaped tumour located in the paramedian region of the mandibular body, size 3cm. The lesion caused mobility of the teeth within the tumour site, without affecting adjacent teeth. Complete surgical excision resulted in a moderate bone defect.

3.2. Histopathological Aspects

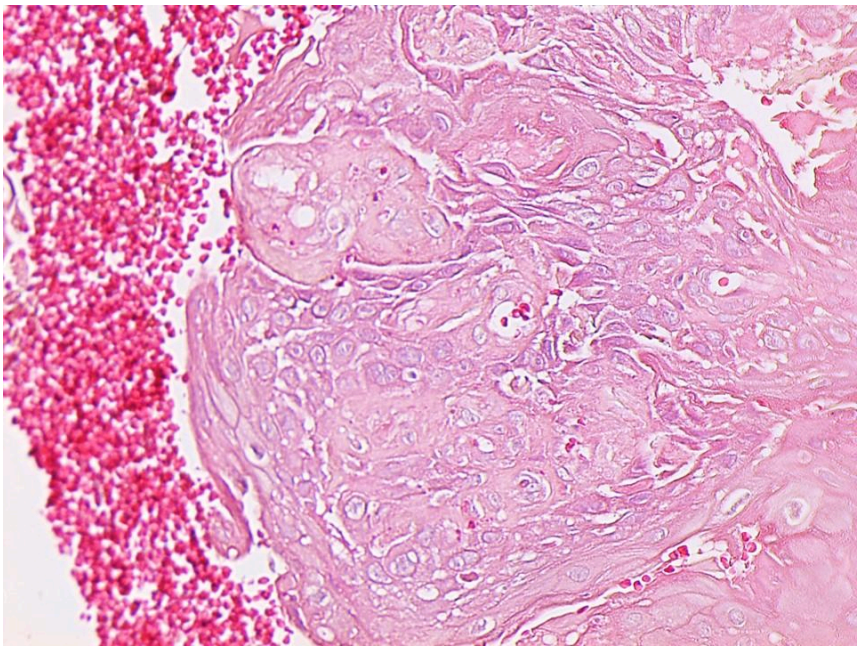

Figure 7. Well-differentiated squamous cell carcinoma – characterised by hyperkeratosis, presence of keratin pearls, minimal inflammatory infiltrate in the lamina propria, and rare mitotic figure

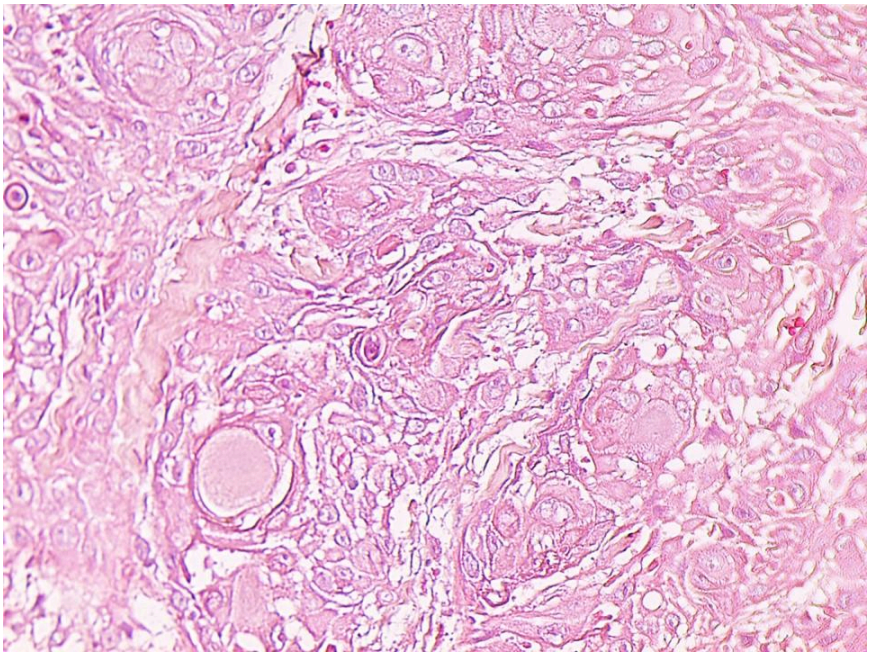

Figure 8. Moderately differentiated squamous cell carcinoma, characterised by the presence of keratin pearls, nuclear pleomorphism, moderate mitotic activity, disorganised architecture, and abundant collagen fibers within the connective tissue

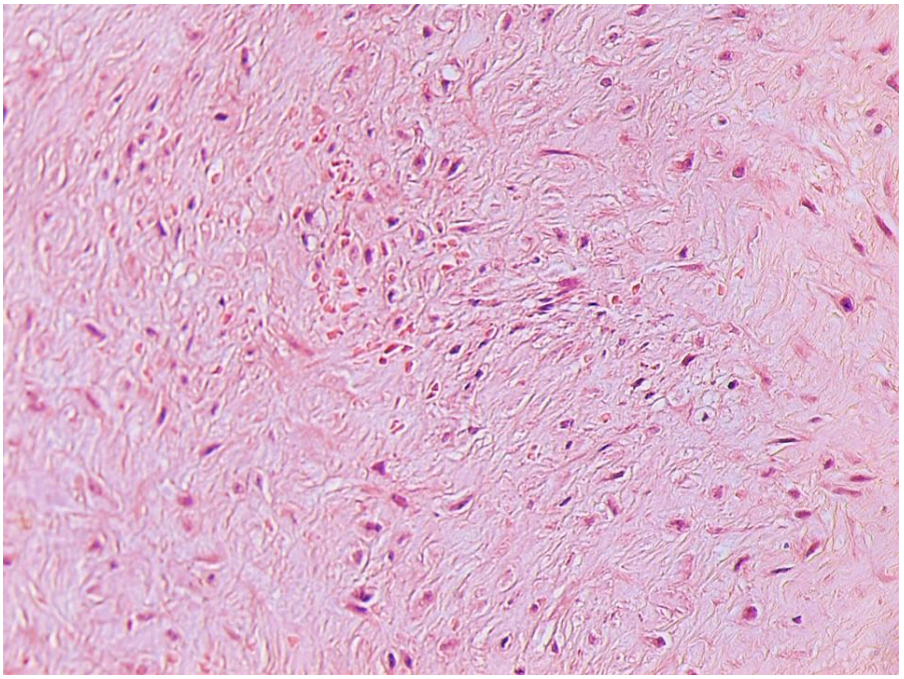

Figure 5. Mandibular mesenchymal tumour – presence of numerous spindle-shaped cells with elongated, hyperchromatic nuclei; scant inflammatory infiltrate in the lamina propria; fibrous stroma.

4. Conclusions

Oral squamous cell carcinoma (OSCC) is a major public health problem worldwide, being the most common form of malignant cancer of the oral cavity. In 2022, an estimated 389,846 new cases of oral cancer were reported, making it the 16th most common cancer worldwide. The highest number of cases were reported in India, China, and the United States, with India alone accounting for 143,759 new cases. Early diagnosis of OSCC is essential in improving the clinical outcome of patients, as late identification of the disease typically results in advanced stages and a poor prognosis. Conventional methods, such as visual examination and biopsy, may be affected by the subjectivity of clinical assessment and delays in establishing a diagnosis.

In this context, artificial intelligence (AI) has recently emerged as an innovative tool in medical diagnosis, offering the possibility of increasing the accuracy, speed, and efficiency of the diagnostic process. The recent development of AI-based technologies has led to significant advances in the identification of OSCC. Machine learning algorithms, especially deep learning models such as convolutional neural networks (CNN), have demonstrated high accuracy in the analysis of imaging and histopathological data. Additionally, automated oral screening systems and computer-aided diagnosis (CAD) platforms have been created that use AI for the automatic classification of lesions, thus reducing the dependence on human interpretation and the time required to establish a diagnosis. The integration of artificial intelligence with digital pathology, radiomics, and multimodal data fusion contributes to improved diagnostic accuracy and opens new perspectives for the detection and personalised management of oral squamous cell carcinoma (OSCC).

Numerous studies have examined the use of artificial intelligence (AI) in the detection of oral squamous cell carcinoma (OSCC). A systematic review and meta-analysis, which included 16 studies and a total of 6,606 samples, evaluated the accuracy of AI-assisted diagnostic methods in identifying OSCC. The results showed a mean sensitivity of 92% and a mean specificity of 91.9%, suggesting that AI-based models can identify OSCC with a high degree of accuracy.

Recent advances also highlight the emerging role of AI-generated biomarkers and predictive analytics tools in predicting the prognosis of patients with OSCC. Artificial intelligence models that integrate genomic and transcriptomic data are being investigated for risk stratification and

personalised therapeutic strategies. In parallel, real-time AI-assisted intraoperative assessment is increasingly being used for the verification of surgical resection margins, contributing to the optimisation of clinical decision-making and postoperative outcomes. However, despite these encouraging results, the implementation of AI in clinical practice for OSCC diagnosis requires further validation through large prospective studies. For these technologies to be widely adopted, it is essential to address existing challenges, such as data standardisation, increasing the transparency and interpretability of models, and their efficient integration into clinical workflows (Chowdhury et al., 2025).

Beyond diagnostic accuracy, the studies reviewed in this article highlight a progressive shift from single-modality, single-task AI systems towards integrated, multimodal frameworks that combine histopathological, radiological, and clinical data. Convolutional neural networks applied to digitised histology, high-resolution in vivo confocal microscopy, radiomics-based CT, MRI, and PET models, together with real-world mandibular OSCC cases, collectively demonstrate that malignant disease is best understood at the intersection of morphology, function, and clinical impact. This triadic perspective—imaging, histological, and neurological/functional assessment—underscores that AI should not replace expert judgement, but rather augment multidisciplinary decision-making by providing quantitative, reproducible, and explainable support.

Future research should therefore prioritise the development of externally validated, prospective AI tools that are seamlessly embedded into clinical workflows, interoperable across institutions, and trained on diverse populations to reduce bias. Equally important will be efforts to improve model interpretability, develop user-friendly interfaces for clinicians, and conduct outcome-based evaluations that demonstrate tangible benefits in survival, functional preservation, and quality of life. In this way, artificial intelligence can evolve from a promising experimental technology into a mature, clinically trusted partner in the comprehensive management of oral squamous cell carcinoma.

References

Ahmad, M., Irfan, M. A., Sadique, U., Haq, I. U., Jan, A., Khattak, M. I., Ghadi, Y. Y., & Aljuaid, H. (2023). Multi-method analysis of histopathological image for early diagnosis of oral squamous cell carcinoma using deep learning and hybrid techniques. *Cancers, 15*(21), 5247. https://doi.org/10.3390/cancers15215247

Almangush, A., Mäkitie, A. A., Triantafyllou, A., de Bree, R., Strojan, P., Rinaldo, A., & Ferlito, A. (2020). Staging and grading of oral squamous cell carcinoma: An update. *Oral Oncology, 107*, 104799. https://doi.org/10.1016/j.oraloncology.2020.104799

Batsakis, J. G. (1985). Pathology of head and neck tumors: Perineural spread. *Annals of Otology, Rhinology & Laryngology, 94*(5), 426–428.

Chamoli, A., Gosavi, A. S., Shirwadkar, U. P., Wangdale, K. V., Behera, S. K., Kurrey, N. K., & Dandekar, S. P. (2021). Overview of oral cavity squamous cell carcinoma: Risk factors, mechanisms, and diagnostics. *Oral Oncology, 121*, 105451. https://doi.org/10.1016/j.oraloncology.2021.105451

Chowdhury, T., Kasralikar, P., Syed, A. A., Tumati, R., Patel, S., & Kommineni, D. (2025). Role of artificial intelligence in the diagnosis of oral squamous cell carcinoma: A systematic review. *Cureus, 17*(4), e81800. https://doi.org/10.7759/cureus.81800

Deng, C., Hu, J., Tang, P., Xu, T., He, L., Zeng, Z., & Sheng, J. (2024). Application of CT and MRI images based on artificial intelligence to predict lymph node metastases in patients with oral squamous cell carcinoma: A subgroup meta-analysis. *Frontiers in Oncology, 14*, 1395159. https://doi.org/10.3389/fonc.2024.1395159

Dropkin, M. J. (1999). Body image and quality of life after head and neck cancer surgery. *Cancer Practice, 7*(6), 309–313. https://doi.org/10.1046/j.1523-5394.1999.76006.x

Evans, M., Bonomo, P., Chan, P. C., Chua, M. L. K., Eriksen, J. G., Hunter, K., & Nutting, C. (2025). Post-operative radiotherapy for oral cavity squamous cell carcinoma: Review of the

data guiding the selection and the delineation of post-operative target volumes. *Radiotherapy and Oncology, 207*, 110880. https://doi.org/10.1016/j.radonc.2025.110880

Ghanaati, S., Udeabor, S. E., Winter, A., Sader, R., & Heselich, A. (2025). Cancer recurrence in operated primary oral squamous cell carcinoma patients seems to be independent of the currently available postoperative therapeutic approach: A retrospective clinical study. *Current Oncology, 32*(4), 208. https://doi.org/10.3390/curroncol32040208

Gokavarapu, S., Chandrasekhara Rao, L. M., Patnaik, S. C., Parvataneni, N., Raju, K. V., & Chander, R. (2015). Prognostic value of frozen section in T1, T2 carcinoma of oral cavity. *Indian Journal of Otolaryngology and Head & Neck Surgery, 67*(Suppl 1), 86–90. https://doi.org/10.1007/s12070-014-0783-6

Hammerlid, E., & Bjordal, K. (2001). A prospective study of quality of life in head and neck cancer patients. *Head & Neck, 23*(7), 544–555.

Huang, S. H., & O'Sullivan, B. (2013). Oral cancer: Current role of radiotherapy and chemotherapy. *Medicina Oral, Patología Oral y Cirugía Bucal, 18*(2), e233–e240. https://doi.org/10.4317/medoral.18772

Liebig, C., Ayala, G., Wilks, J. A., Berger, D. H., & Albo, D. (2009). Perineural invasion in cancer: A review of the literature. *Cancer, 115*(15), 3379–3391. https://doi.org/10.1002/cncr.24396

Montero, P. H., Yu, C., Palmer, F. L., Patel, P. D., Ganly, I., Shah, J. P., & Patel, S. G. (2014). Nomograms for preoperative prediction of prognosis in patients with oral cavity squamous cell carcinoma. *Cancer, 120*(2), 214–221. https://doi.org/10.1002/cncr.28407

Oya, K., Kokomoto, K., Nozaki, K., & Toyosawa, S. (2023). Oral squamous cell carcinoma diagnosis in digitized histological images using convolutional neural network. *Journal of Dental Sciences, 18*(1), 322–329. https://doi.org/10.1016/j.jds.2022.08.017

Öztürk, E. M. A., Ünsal, G., Erişir, F., & Orhan, K. (2024). Prediction of bone invasion of oral squamous cell carcinoma using a magnetic resonance imaging-based machine learning model. *European Archives of Oto-Rhino-Laryngology, 281*(12), 6585–6597. https://doi.org/10.1007/s00405-024-08862-z

Passchier, E., Beck, A. C. C., Stuiver, M. M., Retel, V. P., Navran, A., van Harten, W. H., & van der Molen, L. (2024). Organization of head and neck cancer rehabilitation care: A national survey among healthcare professionals in Dutch head and neck cancer centers. *European Archives of Oto-Rhino-Laryngology, 281*(5), 2575–2585. https://doi.org/10.1007/s00405-024-08488-1

Patel, S. G., & Lydiatt, W. M. (2008). Staging of head and neck cancers: Is it time to change the balance between the ideal and the practical? *Journal of Surgical Oncology, 97*(8), 653–657. https://doi.org/10.1002/jso.21021

Pfaehler, E., Schindele, A., Dierks, A., Busse, C., Brumberg, J., Kübler, A. C., Buck, A. K., Linz, C., Lapa, C., Brands, R. C., & Kertels, O. (2025). Value of PET radiomic features for diagnosis and recurrence prediction of newly diagnosed oral squamous cell carcinoma. *Scientific Reports, 15*(1), 17475. https://doi.org/10.1038/s41598-025-02305-3

Rahadiani, N., Habiburrahman, M., Handjari, D. R., Stephanie, M., & Krisnuhoni, E. (2022). Clinicopathological characteristics predicting advanced stage and surgical margin invasion of oral squamous cell carcinoma: A single-center study on 10 years of cancer registry data. *Oncology Letters, 24*(4), 364. https://doi.org/10.3892/ol.2022.13484

Ramani, R. S., Tan, I., Bussau, L., O'Reilly, L. A., Silke, J., Angel, C., Celentano, A., Whitehead, L., McCullough, M., & Yap, T. (2025). Convolutional neural networks for accurate real-time diagnosis of oral epithelial dysplasia and oral squamous cell carcinoma using high-resolution in vivo confocal microscopy. *Scientific Reports, 15*, 2555. https://doi.org/10.1038/s41598-025-86400-5

Rogers, S. N., Lowe, D., Fisher, S. E., Brown, J. S., & Vaughan, E. D. (2008). Health-related quality of life and clinical function after mandibular resection and reconstruction for oral cancer. *British Journal of Oral and Maxillofacial Surgery, 46*(4), 273–279.

Sharma, S., Kumar Upadhyay, A., Prakash, A., Singodia, P., Ravi Kiran, S., & Shankar, R. (2024). Treatment complications of head and neck cancers and rehabilitation measures: A narrative review. *Cureus, 16*(5), e61173. https://doi.org/10.7759/cureus.61173

Szyfter, K. (2021). Genetics and molecular biology of head and neck cancer. *Biomolecules, 11*(9), 1293. https://doi.org/10.3390/biom11091293

Taberna, M., Gil Moncayo, F., Jane-Salas, E., Antonio, M., Arribas, L., Vilajosana, E., & Mesia, R. (2020). The multidisciplinary team (MDT) approach and quality of care. *Frontiers in Oncology, 10*, 85. https://doi.org/10.3389/fonc.2020.00085

Wreesmann, V. B., Katabi, N., Palmer, F. L., Montero, P. H., Migliacci, J. C., Gonen, M., & Patel, S. G. (2016). Influence of extracapsular nodal spread extent on prognosis of oral squamous cell carcinoma. *Head & Neck, 38*(Suppl 1), E1192–E1199. https://doi.org/10.1002/hed.24190