

# Surgical pathology of oral cancer

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## Abstract

Oral squamous cell carcinoma (OSCC) is a well-documented form of malignancy with established aetiological risk factors that remains a global burden. Trends show an increased incidence in developing countries despite advances in therapeutic management and disease control. The morbidity and mortality associated with OSCC are significant public health concerns. This review examines the histopathological variants of OSCC and accentuates clinicopathological features with prognostic significance. Furthermore it highlights critical surgical pathological elements which are to be included in the diagnostic report.

**Keywords** histopathology; oral cancer; oral cavity; squamous cell carcinoma

## Introduction

Oral cancer is diagnosed histopathologically as squamous cell carcinoma in the overwhelming majority of cases, the two terms thus often being interchangeably applied.

Cancer has rapidly secured its spot second only to cardiovascular disease in global causes of mortality particularly in the last two decades. In 2015 alone, close to 15 million new cases were identified and almost 9 million deaths were reported. Oral and oropharyngeal cancer constituted 529,500 new cancer diagnoses with 292,300 associated deaths reported in 2012 representing almost 3,8% of all cancer diagnoses and 3,6% of all cancer deaths.<sup>1</sup>

The annual incidence of OC including cancer of the lower lip, is estimated at around 3–400,000, the majority of which are diagnosed in developing countries where more than 80% of the world population lives.<sup>1</sup> Geographical and social variation in aetiological risk factors remains the most significant determinant of disease incidence between developed and developing countries. Exposure to lifestyle risk factors such as tobacco use and alcohol consumption remain the most well-established causes of oral cancer in developed countries as reported in the literature from the United States. Public awareness campaigns have

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resulted in an overall decrease in the incidence of oral cancer in many of these regions. Conversely, developing regions such as Asia attribute an increased incidence to the increased association with cultural habits including the use of betel quid or any of its substitutes. Geographical differences are exemplified by the gender differences with a five-fold increase in OC incidence reported in Taiwanese male patients over the last 25-years.<sup>2</sup>

The 5-year survival rate of patients diagnosed with oral cancer remains poor. This is complicated by the development of second primary tumours within genetically altered fields.

## Risk factors

Smoking, smokeless tobacco use (including betel quid chewing) and alcohol consumption are well-documented lifestyle risk factors for the development of oral cancer.<sup>3</sup> Betel quid use is especially prevalent in developing countries of Southeast Asia, whereas in western countries the biggest risk is attributed to tobacco and alcohol consumption, the combined effects of which are synergistic.<sup>4</sup> Although Human papillomavirus infection has been proven as a causal factor in a subset of oropharyngeal carcinomas, its role if any in OSCC, however, remains to be clarified.<sup>5,6</sup>

## Histopathology report

Several clinicopathological characteristics of OSCC may influence tumour prognosis and overall survival. These factors should therefore be systematically included in histopathological diagnostic reports. The Royal College of Pathologists has published detailed guidelines of essential data that should be routinely included in histopathology reports of carcinomas of the head and neck region for the purpose of standardisation.<sup>7</sup> A summary of the essential data is presented in Table 1 that forms the basis of the discussion that follows.

## Tumour site

The association between anatomical site and patient prognosis is predominantly related to the development of regional metastases. Tumours originating in posterior regions of the oral cavity have a greater propensity for development of cervical lymph node and distant metastases compared with tumours from the anterior part of the oral cavity.<sup>8,9</sup> Squamous cell carcinoma (SCC) of the tongue is associated with a poor survival compared with tumours at other intra-oral sites and higher metastatic rates have been reported for base of tongue tumours compared with anterior tongue tumours.<sup>10</sup> The density of lymphatic vessels within and towards the base of tongue compared with the density of vessels in the tip of tongue may be the underlying cause of such differences.<sup>11</sup> Tumours that cross the midline or those located close to its proximity are more frequently associated with bilateral neck metastases. The presence or absence of metastatic disease as well as its extent of involvement have significant prognostic and therapeutic implications.<sup>12</sup> Posterior anatomical sites present additional surgical challenges in pursuit of margins free of involvement.<sup>13</sup>

## Tumour diameter and depth of invasion

Tumour diameter is based on clinical measurement unless the histological measurement is greater. Tumour diameter remains

**Core data that should be provided in histopathology reports of specimens of squamous cell carcinoma originating in the head and neck area based on the guidelines from the Royal College of Pathologists, London<sup>7</sup>**

Primary tumour information	<ul style="list-style-type: none"> <li>• Tumour site</li> <li>• Tumour diameter and depth of invasion</li> <li>• Histological subtype with degree of differentiation</li> <li>• Pattern of invasion at invasive front</li> <li>• Mucosal and deep margin status</li> <li>• Vascular, neural or bone invasion</li> <li>• Degree of dysplasia at margin</li> <li>• DNA ploidy</li> </ul>
Neck dissection information	<ul style="list-style-type: none"> <li>• Number of nodes found in different levels</li> <li>• Number and level of nodes with metastases</li> <li>• Size of largest metastasis</li> <li>• Presence of extracapsular spread</li> </ul>

**Table 1**

critical to determine treatment modality and correlates strongly with both risk of regional metastatic disease and overall survival.<sup>9</sup>

Depth of invasion is determined histologically and in spite of tissue shrinkage following fixation and processing, is prognostically more accurate than tumour diameter.<sup>9</sup> When ulceration is present, the depth of invasion is measured from where the mucosa would have been or adjacent to any normal non-ulcerated mucosa present. Care should be taken to include individual tumour cells within the depth of the surgical specimen. Depth of invasion strongly predicts cervical lymph node metastasis at a cut-off of 4 mm.<sup>14</sup> In tumours of the tongue, the accepted cut-off is 8 mm.<sup>15</sup> This was previously determined histologically in the absence of fixation artefact. In addition, a depth of invasion of 4 mm has strong predictive value for occult regional metastases and is an indication for elective neck treatment. Tumour depth of invasion is measured in mm and represents a general “cut-off” figure for each anatomical site. The critical thickness for tumours occurring in the floor of mouth and ventral tongue is accepted as less than 4 mm<sup>16</sup>

### Histological subtypes

#### Verrucous carcinoma

Verrucous carcinoma (VC) is a low-grade variant of OSCC found predominantly in older patients of male gender. The mandibular buccal sulcus area and alveolar ridge represent the most commonly involved sites. The clinical presentation of lesions is reflected in their histology. These features are dominated by prominent hyperkeratosis of the hyperplastic epithelium surfacing papillary and verrucous processes. The infiltrating border of tumours comprises bulbous rete processes that push rather than slice into the underlying connective tissue. A polymorphous chronic inflammatory cell infiltrate is frequently noted at the tumour front. Cellular atypia of the neoplastic cells is characteristically absent with isolated atypical cells limited to the basal zones if present (Figure 1). The

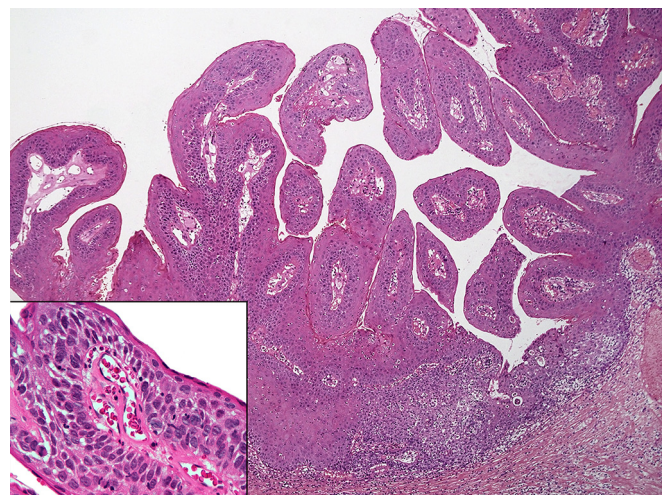


**Figure 1** Verrucous carcinoma is characterised by papillary processes with hyperparakeratosis and blunt elongated rete processes. Insert: Lack of atypia in blunt processes.

degree and extent of the atypia identified in conventional squamous cell carcinoma should not be present. Up to 20% of verrucous carcinomas harbour areas of conventional SCC, the possibility of which, requires adequate tumour sampling due to prognostic differences between these two subtypes.<sup>9</sup> The histopathological differential diagnosis for verrucous carcinoma includes verrucous hyperplasia and papillary SCC. The increased thickness of the infiltrative epithelial component in comparison to that of adjacent normal epithelium is of assistance to separate VC from verrucous hyperplasia whilst the lack of papillary projections and cytological atypia separate it from papillary SCC.

#### Papillary squamous cell carcinoma

Papillary squamous cell carcinoma (PSCC) is a recently described variant of SCC with an exophytic growth pattern. It occurs more frequently in the larynx and hypopharynx but is well documented in the oral cavity. The papillary nature of the tumour is



**Figure 2** Finger-like projections with a fibrovascular core of a papillary squamous cell carcinoma. Insert: Cytological atypia is clearly evident.

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