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Oral Cancer

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ABSTRACT

The management of oral cancer is a multidisciplinary endeavour, as each patient presents the treating clinicians with a unique set of challenges the management of which impacts on both survival and quality of life. This article focuses on the management of oral cancer. We highlight the epidemiology and risk factors for oral cancer in Australia, the various clinical presentations that occur and the staging of oral cancer. In the vast majority of cases surgery remains the mainstay of treatment. Radiation and medical oncology is usually used in an adjuvant context. Dental professionals play a critical role in many stages of management from the initial detection, to optimising pre treatment dental health and managing the short and long term sequelae of treatment. Monitouring for recurrence and the development of second primary tumours is a key role.

Keywords: Cancer outcomes, chemotherapy, epidemiology, head and neck tumours, oral cancer, radiotherapy, surgery.

Abbreviations and acronyms: AJCC = American Joint Commission of Cancer; CT = Computer tomography; ENE = Extra-nodal extension; H & N = Head and neck; MDT = Multidisciplinary team; MRI = Magnetic Resonance imaging; OPG = Orthopantogram; PEG = Percutaneous endoscopic gastrostomy; PET = Positron emission tomography; SCC = Squamous cell carcinoma; TMN = Tumour (T), nodal (N), metastasis (M) classification; US = Ultrasound.

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INTRODUCTION

Every patient with oral cancer presents the treating clinician with a unique set of challenging, complex and multidisciplinary clinical problems, the solutions to which impact both their survival and quality of life. The management of all oral cavity cancers should occur in a Multidisciplinary Head and Neck Oncology Team. There are many different clinicians that form part of the Head and Neck Multidisciplinary Team (H&N MDT), and these include (but are not limited to): oral and maxillofacial, ear, nose and throat and plastic & reconstructive surgeons, radiation oncologists, medical oncologists, radiologists, anatomical pathologists, anaesthetists, speech and language therapists, dieticians, head and neck nurses, physiotherapists, oral medicine specialists, prosthodontists, special needs dentists, facial prosthetists and social workers.

The management of cancers of the oral cavity is complex, due to the functional and aesthetic implications of treatment of tumours in this region. Breathing, speech, deglutition, sight, smell, taste, mastication and jaw function, are just several of the critical functions of the head and neck that can be impaired, either temporarily or permanently by the tumour or its treatment. In addition, our facial and dental aesthetics are important in how we are perceived by others; self-esteem and self-confidence may be severely affected by the tumour itself and/or its treatment.

Dentists play a critical role in the management of oral cancer, from the detection of premalignant lesions, early detection of oral cancer, management of the oral cancer patient's dentition both prior to and post definitive treatment, surveillance of recurrent or new primary tumours in conjuction with the treating specialist, and rehabilitation of missing teeth in conjunction with the treating maxillofacial surgeon and prosthodontist.

DEFINITIONS

The oral cavity is defined as the anatomical space which lies between an imaginary coronal plane drawn from the junction of the soft and hard palate and the circumvallate papillae of the tongue to the vermillion of the lips. There are seven oral cavity subsites that are used to classify the oral cavity cancer (lip, tongue, floor of mouth, buccal, hard palate, alveolar, retromolar trigone and soft palate) (Fig. 1).

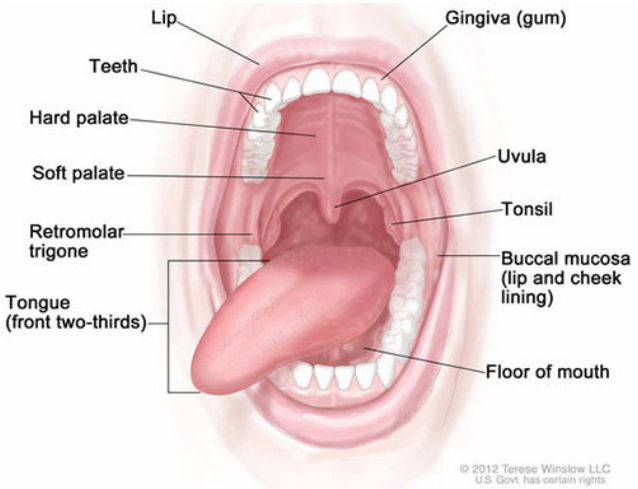


Fig. 1 The seven oral cavity subsites.

EPIDEMIOLOGY

In Australia, there are more than 4000 new cases of head and neck cancers (including lip) diagnosed every year.[1] Over 600 of these cancers are oral cavity cancers. Oral cavity cancer is a highly lethal disease with a mortality rate that approaches 50%. The vast majority of oral cavity cancers are squamous cell carcinomas (SCC), other types of oral cavity cancers such as minor salivary gland malignancies, sarcomas, malignant odontogenic tumours, melanoma and lymphoma comprise less than 10% of oral cavity cancers. Dentists and dental specialists are the common referring clinicians for a patient with oral cancer.

RISK FACTORS

Smoking and excessive alcohol intake (>5 standard drinks/day) are regarded as the main risk factors for the development of oral SCC in Australia. Smoking confers a 7 × relative risk of the development of oral SCC and alcohol intake of >50 g/day confers a 6 × relative risk of developing oral cancer.[2] In subcontinental countries, betel nut chewing is an important risk factor in the development of oral cancer, where oral cancers represent almost 50% of all total cancer diagnoses (compared with <1% in Australia). There is an additional subgroup of non-smoking non-drinking mostly middle age female patients who are also recognised.[3]

CLINICAL PRESENTATION

The clinical presentation of oral cancer is highly variable, and the presentation of oral cavity cancer is most often related to the primary tumour, with symptoms and signs from cervical or distant metastases much less common. Any oral cavity lesion, which fails to resolve in 2–3 weeks, should raise the suspicion of the treating clinician (Fig. 2).

The most common presentations are that of an ulcerated lesion in the oral cavity, patients may also present with mobile teeth, bleeding, pain or numbness in the mouth or face or an ill fitting dental prosthesis.

White lesions of the oral cavity can represent a variety of diagnoses, including frictional keratosis, oral lichen planus and viral lesions such as warts. However, even 'benign' appearing white lesions can be dysplastic or even frankly malignant on biopsy (Fig. 3).

Erythematous lesions must also raise suspicion of an oral cancer. In most studies, the incidence of an oral cancer/carcinoma in-situ on biopsy of erythroplakia approaches 50%[4] (Fig. 4).

Lesions that are exophytic, proliferative or papillomatous (wart like) can also be presentations of oral cancer (Fig. 5).

Less commonly, oral cavity cancers can present as a cystic lesion around a tooth, which mimics that of an odontogenic cyst. This is the preoperative OPG of a patient with a radiolucent lesion around the impacted

Fig. 2 Squamous cell cancer of the tongue.

Fig. 3 White lesions.

Fig. 4 Erythematous lesion.

Fig. 5 Exophytic lesion.

38 extending to the 37 which on biopsy was a SCC (Fig. 6).

Alternatively, a non healing extraction socket (>6 weeks) should also raise suspicion of a possible alveolar carcinoma (Fig. 7).

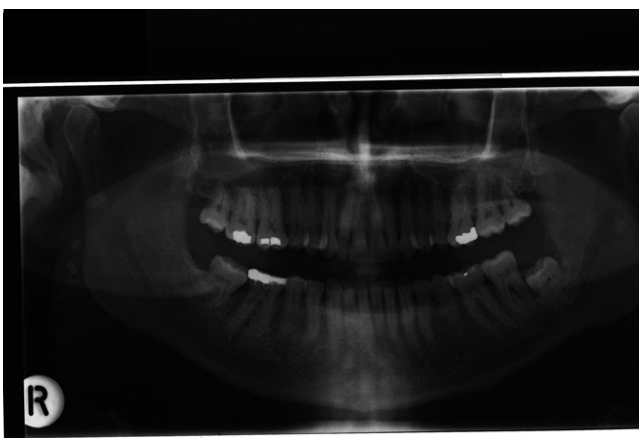


Fig. 6 Cystic lesions.

Fig. 7 Non healing extraction socket.

Presentations of other oral cavity cancers apart from SCC can include a pigmented lesion (oral melanoma) (Fig. 8).

If there is any suspicion of a lesion that may represent oral cavity cancer, the lesion site and size should be documented, a clinical photograph taken if possible, and urgent referral made to an Oral & Maxillofacial Surgeon who is involved in a Head and Neck Oncology MDT.

DIAGNOSIS AND STAGING

The diagnosis of oral cancer is dependent on obtaining a sample of tissue from the lesion, a biopsy. Ideally, the biopsy should be done by an Oral & Maxillofacial Surgeon as the treating surgeon has the opportunity to complete a full head and neck examination, including exact measurements, palpation of lesion thickness and clinical examination of the

Fig. 8 Pigmented lesion.

cervical nodes ± clinical photography and in select situations, even obtain some imaging prior to distortion of the lesion through post biopsy changes. This is especially true for early tumours of the oral cavity where the depth of the lesion can be difficult to determine on post-biopsy imaging due to tissue oedema. Broadly speaking, there are 2 types of biopsies that can be employed, incisional and excisional. In almost all situations, an *incisional* biopsy is favoured, at the margin of the lesion with 'normal' tissue, at an adequate depth for the pathologist to assess invasion of the tumour (SCC) through the lamina propria. The diagnosis of other malignancies in the oral cavity (e.g. lymphoma) may require not just histopathologic analysis (biopsy in formalin), but require fresh tissue to be sent for additional tests (e.g. flow cytometry).

A critical component in the diagnosis of oral cancer is the histopathologic analysis by an anatomic pathologist. All maxillofacial surgeons involved with oral cancer will have a close relationship with an anatomical pathologist who has a detailed knowledge of oral pathology, as there can be differences in the interpretation of a biopsy amongst pathologists. Additionally, the treating surgeon will always maintain a low threshold for re-biopsy if the clinical behaviour of the lesion is not in accordance with the 'diagnosis' from the initial biopsy.

Once the tissue diagnosis has been established, the treating surgeon will arrange appropriate radiologic scans to radiologically stage the tumour: i.e. to assess the primary tumour dimensions and invasion of adjacent structures, cervical node involvement, and whether there are distant metastases. The imaging modalities commonly used in oral cancer evaluation are computed tomography (CT), magnetic resonance imaging (MRI), ultrasound (US) and positron emission tomography (PET) to stage the cancer. An orthopantomogram (OPG) is useful for assessment of the dentition as well as evaluation of mandibular height in the event that part of the mandible will need to be removed due to involvement or close proximity to the cancer.

CT scans of the head/neck/chest are routinely employed in assessment of oral cancer and are excellent in highlight cortical destruction, potential cervical node metastases and pulmonary metastases (Figs 9–11).

MRI of the neck is excellent at evaluating the soft tissue extent of the tumour, extent of marrow infiltration of the mandible or maxilla and assessment of intra or perineural involvement (Figs 12 and 13).

Ultrasound, used either intraorally for accessible tumours, or more commonly for assessment of cervical nodes can be combined with a fine-needle aspirate for cytologic assessment of suspicious cervical nodes (Fig. 14).

Fig. 9 Axial CT of the mandible with bone windows showing cortical destruction of the right body of the mandible from a SCC (NB amalgam artefect).

PET is often combined with an anatomical imaging modality (CT or MR), and is a functional scan, where a radiotracer is administered intravenously to the

Fig. 10 Axial CT of the neck with contrast showing multiple heterogenous, enhancing, round right cervical nodes suspicious for nodal metastases.

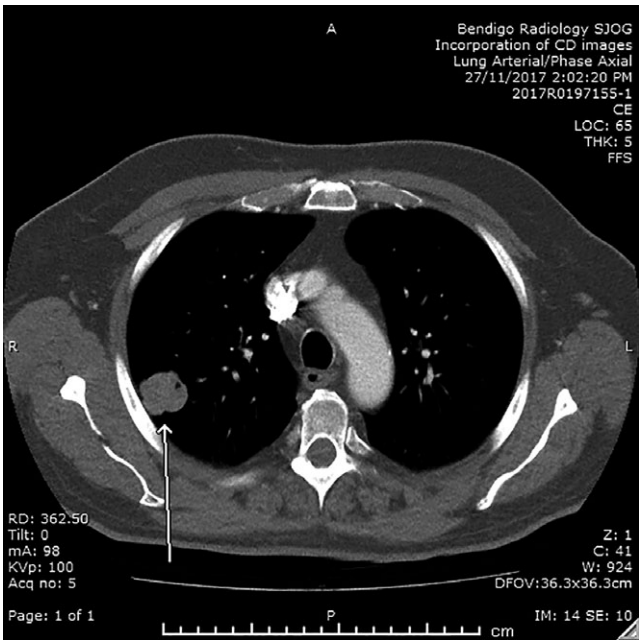


Fig. 11 Axial CT of the chest showing a suspicious lesion in the right lung, which could represent a pulmonary metastasis from oral cancer, but could also represent a synchronous new lung cancer.

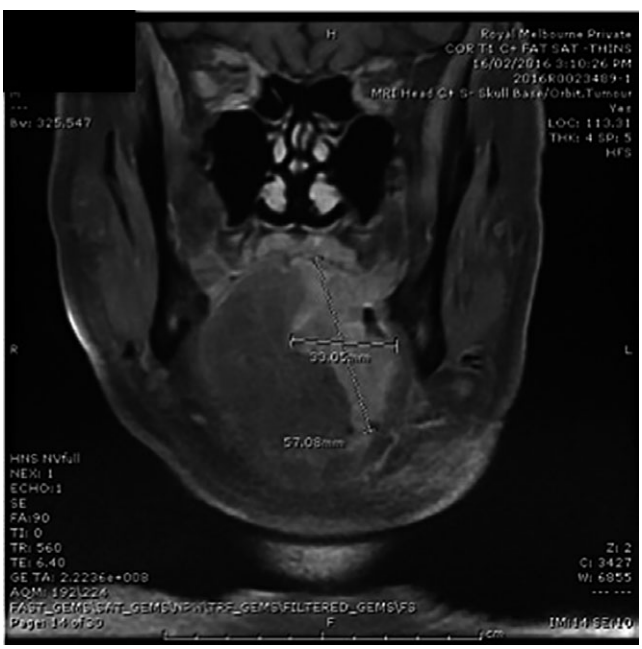


Fig. 12 Coronal MR slice showing the depth and height of the left tongue/floor of mouth SCC.

patient; the tracer is preferentially taken up by cells with a high metabolic rate (a characteristic of many oral cancers). Infection and inflammation however can also provide similar radiologic appearances. It is most often used in advanced (stage 3 or 4 disease, or in salvage/recurrent cases) and the assessment of metastatic disease (Figs 15a and 15b.

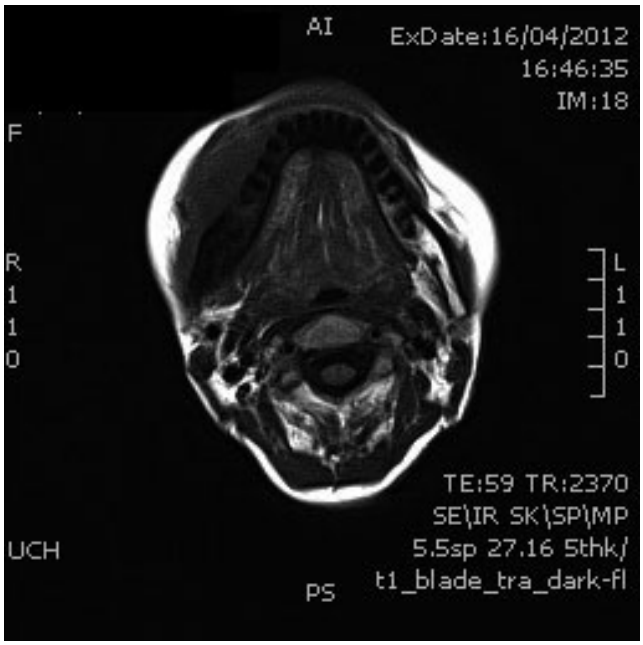


Fig. 13 Axial MR showing extensive marrow signal change of the mandible from the right ramus to the left second premolar region.

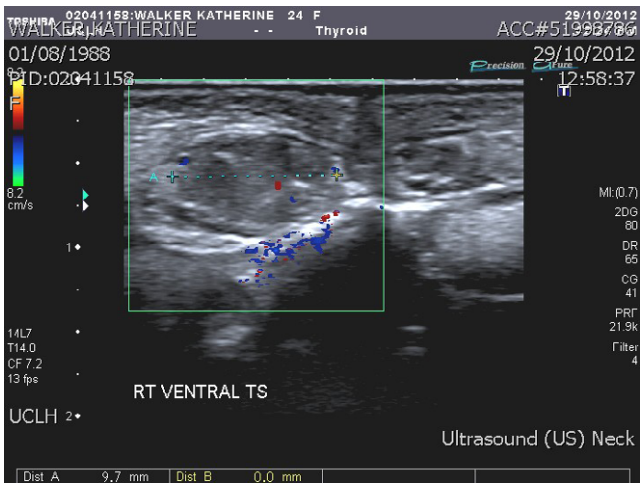


Fig. 14 US of the tongue measuring the dimensions of the tongue tumour (in this case adenoid cystic carcinoma). The depth measurement is particularly helpful.

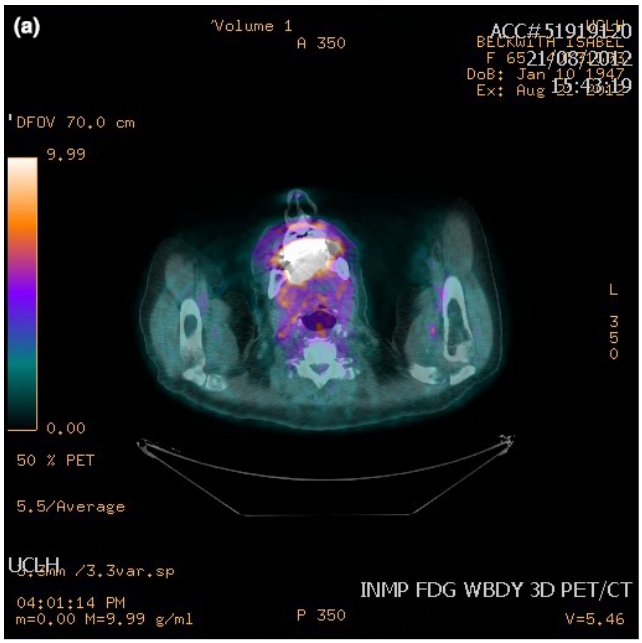
STAGING

Staging is completed according to the American Joint Commission of Cancer (AJCC) Cancer Staging Manual (version 8 which is described below will be used from 1st January 2018).[5]

Staging of the oral cavity cancer follows the TNM classification: T = tumour, N = nodal status, M = metastases (Fig 16).

TUMOUR

Tumour stage has traditionally referred to the maximum radial dimension of the tumour, but in the latest



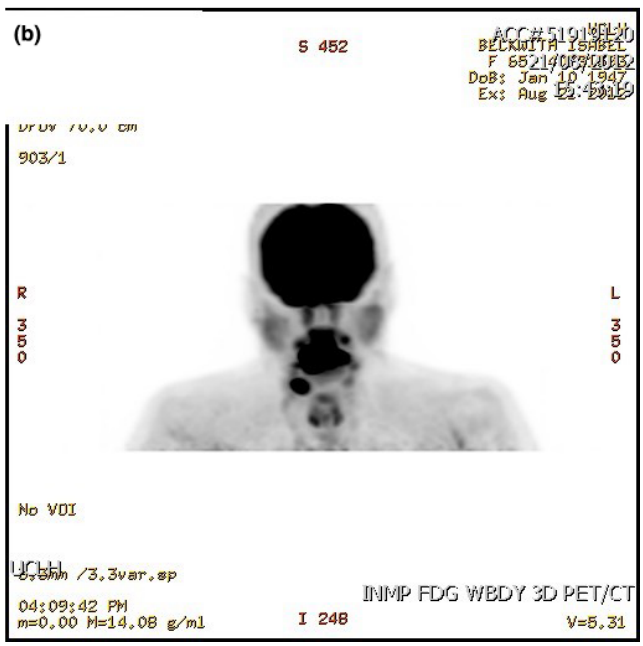


Fig. 15 (a) and (b). PET-CT showing extensive uptake in the floor of mouth and bilateral cervical nodes (R≫L) from a large T4 SCC of the anterior floor of mouth.

classification, the depth of the tumour also affects the T stage (Tables 1 and 2).

Accurate tumour staging is vital to determine the type of treatment offered (curative vs. palliative), the 'field' of treatment (extent of resection for surgical treatment and area of radiation therapy for radiation treatment) as well as providing important information for treating clinicians and patients regarding the prognosis of their disease.

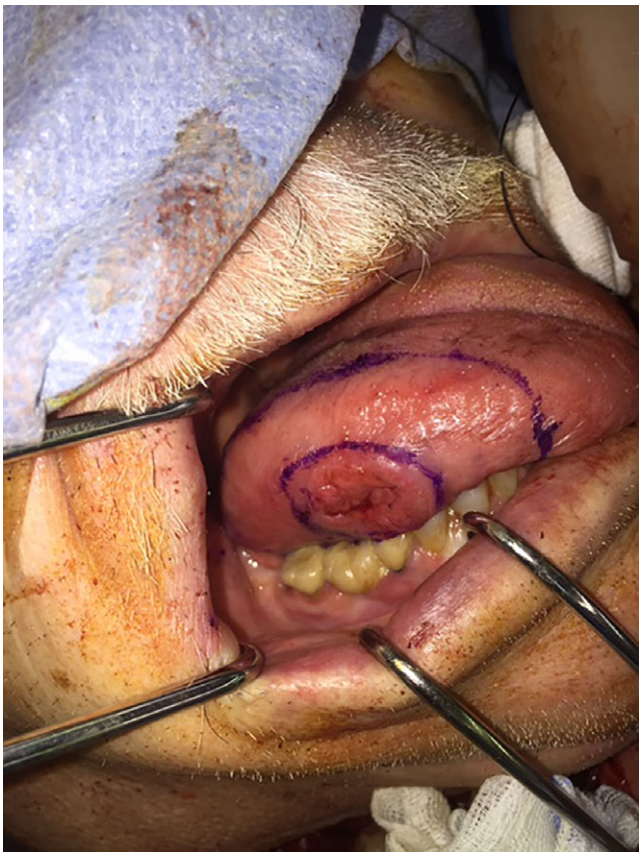


Fig. 16 Inner purple ring is the intraoperative assessment of the extent of the tumour, outer purple ring is the intended resection area.

Table 1. Oral cavity

T0 deleted
T1: size ≤2 cm and DOI ≤5 mm
T2: size ≤2 cm and DOI 5–10 mm or
Size 2–4 cm and DOI ≤10 mm
T3: size >4 cm or >10 mm DOI
T4a extrinsic tongue muscle infiltration
Now deleted

DOI, depth of invasion.

PRINCIPLES OF MANAGEMENT

Every patient with oral cancer should be presented at a Multidisciplinary Tumour Meeting in order that the appropriate, individualised and optimal treatment plan is offered to each and every patient. MDT's have been shown to significantly improve patient outcomes.[3] The MDT framework allows multiple specialists and clinicians to provide input into each patient's treatment plan, allowing improved decision making, adherence to best clinical practice guidelines and the ability to also limit the impact of treatment on the patients quality of life (speech, swallow, mastication etc.).

Table 2. Nodal status

N Category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node mets
N1	Mets in single ipsilateral node ≤3 cm in greatest dimension and ENE(−)
N2a	Mets in single ipsilateral or contralateral node >3 cm but ≤6 cm in greatest dimension and ENE(−)
N2b	Met in multiple ipsilateral nodes, none >6 cm in greatest dimension and ENE(−)
N2c	Met in bilateral or contralateral nodes, none >6 cm in greatest dimension and ENE(−)
N3a	Met in a node >6 cm in greatest dimension and ENE(−)
N3b	Met in single ipsilateral node ENE(+) *or* mutiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+)

ENE, extranodal extension.
Metastases
M0, no distant metastases; M1, distant metastases.

The format of each multidisciplinary meeting varies slightly between institutions, but the common elements are that the spectrum of clinicians involved in the treatment of the patient examine the patient, discuss and view the radiology and pathologic specimens/results and arrive at an individualised management plan for the patient. The first treatment decision in each patients management plan is to determine whether curative or palliative treatment is offered to the patient. In the management of oral cavity cancer, curative treatment is offered if the disease is surgically resectable and confined to the primary site ± cervical nodes. Potentially curative treatment in oral SCC involves surgery with the possibility of adjuvant therapy (radiation therapy or chemoradiation therapy). Once oral SCC has spread to distant sites (e.g. lungs), or is surgically unresectable at the primary/cervical nodal sites due to the involvement of vital structures, then palliative treatment is offered.

Many other factors apart from the type, stage and location of the oral cancer influence the proposed management plan, in particular the patients systemic health and nutritional status and the patients previous treatment in a recurrent oral cancer or 'in-field' new primary. The patients treatment commences from the time of diagnosis, with particular attention paid to optimising their systemic health, nutrition, assessment of perioperative risk (often related to cardiovascular and pulmonary function), management of their medications (e.g. anticoagulants, diabetes medication etc.) and obtaining consent for treatment (discussion about the nature of treatment, benefits and risks of treatment and treatment alternatives). If there is disagreement about the appropriate management plan, then further investigations may be required, or alternatively the management options are discussed with the patient and their family, highlighting the benefits/risks of each particular option and assisting the patient in making their decision. Apart from decision making regarding the treatment of the oral cancer itself, other important treatment decisions surrounding the management of the patient need to be made: type of airway in the peri-operative period (e.g. temporary tracheostomy), route of nutrition (e.g. nasogastric tube vs PEG tube and post-operative treatment setting (ward vs high-dependency unit or intensive care unit).

SURGERY

Surgery remains the primary modality of treatment for oral cancer. Surgery can broadly be divided into 'resective' and 'reconstructive' components. Resective surgery includes the removal of the primary tumour ± management of the cervical nodes ± establishment of a surgical airway (tracheostomy) if required. Reconstructive surgery essentially involves minimising the morbidity of the resection (e.g. replacement of tissue, minimisation of effects on speech, swallow and mastication).

The goal of the resection surgeon is to remove the oral cancer with a margin of normal tissue around the cancer in all 3 dimensions. Current clinical guidelines,[6] recommend that a 5 mm microscopic margin of normal tissue around the tumour should be the goal of the resective surgeon. To obtain a microscopic margin of >5 mm around the tumour, a macroscopic radial margin of 10–15 mm around the tumour is

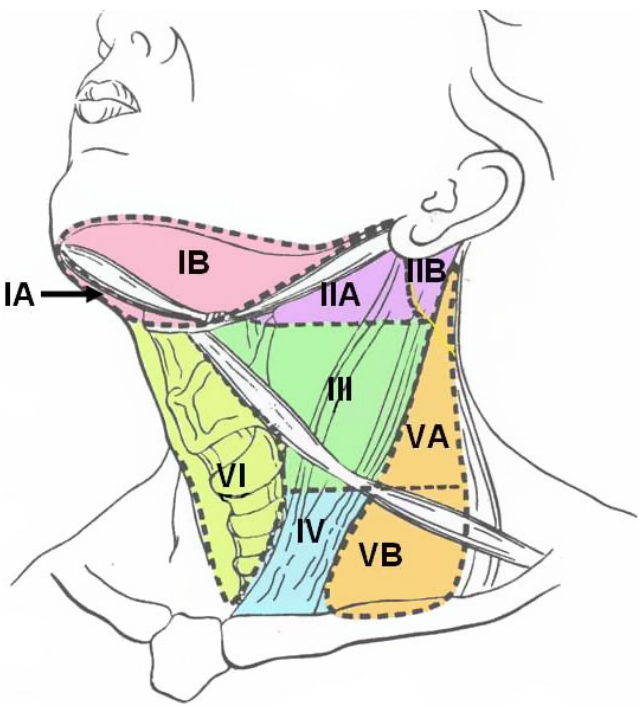


Fig. 17 Neck dissection refers to the removal of cervical lymphatic nodes. Cervical nodes are classified into levels I–VI according to various anatomic boundaries.

marked at the time of surgery, and the deep margin is determined by the preoperative scans and intraoperative palpation. Tumour shrinkage after resection and during pathological preparation is variable depending upon site, and may be as high as 50% (Fig. 17).

The removal of the cervical lymph nodes is the 'neck dissection,' and various types of neck dissections are described depending on the 'levels' of cervical nodes removed and the preservation or sacrifice of certain structures (sternocleidomastoid, internal jugular vein and spinal accessory nerve). The majority of patients with oral cavity SCC will be indicated for a neck dissection, as any oral cavity cancer staged as T2/T3 and T4, and any T1 oral SCC >3 mm thick is recommended for a neck dissection (Fig. 18).[7]

There are several types of neck dissections described, depending on the levels which are dissected and the preservation or sacrifice of certain structures (Table 3 and Fig. 19).[8]

The reconstruction of the surgical defect is then completed and this is well described in the following paper in this supplement.[9,10]

PERIOPERATIVE CARE

The management of the patient in the immediate post-operative period is often complex and is aimed at optimising nutrition, mobilisation, pulmonary function, flap and wound care as well as airway protection, speech and swallow rehabilitation and prevention of complications (flap failure, venous thromboemolism, pulmonary infection, wound infection etc.). Almost all members of the MDT are involved with the post-operative care of the patient, and the quality of this care is critical in achieving successful outcomes for the patient.

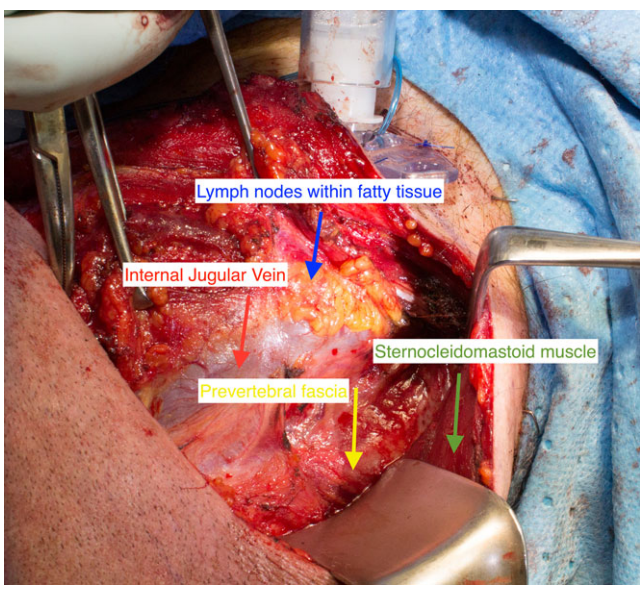


Fig. 18 Dissection of right neck (levels 2, 3 & 4 shown in this photo)

Table 3. Classification of neck dissection[8]

1991 Classification	2001 Classification
1. Radical neck dissection	1. Radical neck dissection
2. Modified radical neck dissection	2. Modified radical neck dissection
3. Selective neck dissection a. Supraomohyoid b. Lateral c. Posterolateral d. Anterior	3. Selective neck dissection: Each variation is depicted by "SND" and the use of parentheses tos denote the levels or sublevels removed
4. Extended neck dissection	4. Extended neck dissection

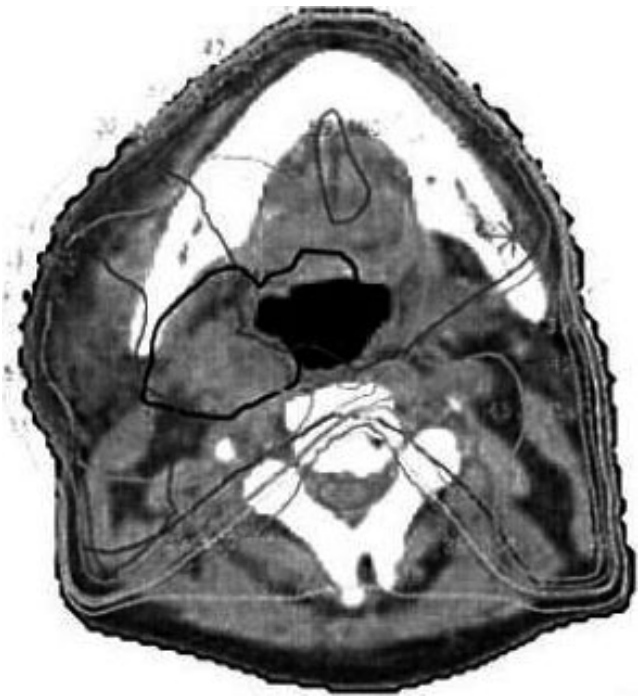


Fig. 19 Example of radiation fields used for curative treatment of a right tonsil carcinoma.

RADIATION THERAPY

Adjuvant post-operative radiation therapy is often indicated in oral cavity cancer, however the treatment decision for this largely depends on the final histopathologic result and stage. Of critical importance is the pathologic staging of the tumour, whether there were positive lymph nodes and the status of the surgical margin. Radiation therapy involves the use of ionising radiation to destroy or damage cancer cells. It is a local treatment, and the 'field' and 'dose' of

ionising radiation is individually determined for each patient. Radiotherapy in oral cancer can be direct at the primary site and/or cervical nodes and can also be used in the management of pulmonary metastases from oral SCC. There are different ways to administer radiation, but the most common form employed in the management of oral cancer is external beam irradiation where the patient lies in a fixed and repeatable position in a machine that produces high energy X-rays which target the specific site/s. Radiation therapy can be used both in the curative and palliative setting, with curative radiation doses significantly higher (e.g. >55–60 Gy) than that which are used in the palliative setting. The dose of radiation is given in fractions, and the treatment period in the curative setting often lasts 6 weeks.

CHEMOTHERAPY

Chemotherapy is added to radiation if extra-capsular extension of the nodal disease is identified. Common drug protocols include cisplatinum or Epidermal Growth Factor inhibitors such as cetuximab. The development of new agents and protocols is ongoing and requires extensive randomised multi-centre studies to determine efficacy before they are introduced.

FOLLOW-UP

Every patient with oral cancer requires long-term follow up. Clinical and/or radiologic surveillance for new and recurrent cancers is important, however in addition, there is often significant morbidity from treatment that requires further rehabilitation and treatment, including but not limited to speech and swallow rehabilitation, the preservation of the remaining dentition and restoration of missing dentition and the management of xerostomia. The psychologic and social morbidity of the cancer diagnosis and treatment must also not be overlooked and should be addressed.

SUMMARY

Oral cavity cancer is a challenging disease with high mortality rates; dentists and dental specialists play a critical role at all stages in the management of patients. Prevention through education about smoking cessation and safe alcohol consumption is critical, detection and early referral of premalignant lesions and oral cancers and ongoing surveillance, follow up and preservation of oral health are just a few of the many roles of the dental practitioner in the management of oral cancer. Each and every patient with oral cancer should be managed within a multidisciplinary team specialised in the management of head and neck tumours and early referral for any suspicious lesion should be made to an Oral and Maxillofacial Surgeon or Oral Medicine Specialist.

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