Imaging patients with cancer of the oral cavity

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Key points

- Highlights that imaging is crucial in the staging of oral cancer.
- Highlights that accurate staging is required so that appropriate treatment can be planned.
- Suggests the common imaging modalities used to stage disease are computed tomography (CT), magnetic resonance imaging (MRI), ultrasound and positron emission tomography-computed tomography (PET-CT).

The staging of oral cavity tumours as with all other malignancy subsites is undergoing a revision in the line with the updated American Joint Committee on Cancer guidelines. Of note, the new guidelines incorporate more emphasis on clinical and histopathological data. The aim of the new guidelines is to increase prognostic concordance between stage and survival. This article aims to review the multimodality approach to imaging of oral cavity malignancy. In addition, it will also review the multidisciplinary approach to diagnosis and management of these tumours as multiple specialities are crucial for effective treatment.

Introduction

Malignancy of the oral cavity, similarly to many other head and neck malignancy subsites, is increasing in prevalence.[1]

The oral cavity is lined by stratified squamous epithelium and is easily inspected clinically.[2] Precise identification of the site of the primary cancer is essential. The anterior border of the oral cavity is the lips. The mylohyoid muscle separates the floor of the mouth and oral cavity from the suprahyoid neck (Fig. 1a). The roof is formed by the hard palate and posterior to it is the oropharyngeal soft palate. At the lateral aspect of the oral cavity is the buccal mucosa and the buccinator muscles. The oral tongue (anterior two thirds of the tongue) sits in the middle of the oral cavity and its junction with the posterior third of the tongue (oropharyngeal tongue) forms the posterior border of the oral cavity (Fig. 1b). The gingival mucosa carpets the maxillary and mandibular alveolar bone and surrounds the teeth. The triangular shaped areas of mucosa posterior to the last mandibular molar teeth are the retromolar trigones.

Most cancers of the oral cavity are squamous cell carcinomas (SCC). Though any oral cavity subsites can be involved, the site most commonly involved by SCC is the oral tongue.[3] Separating the oral tongue from the oropharyngeal tongue (tongue base) is crucial in staging a P16 positive oropharyngeal primary carcinoma. The main aetiology factors for oral cancer are smoking and alcohol. HPV infection seems to be less important as an aetiological factor in oral cancer in comparison to oropharyngeal cancer.[4] Diagnosis is usually

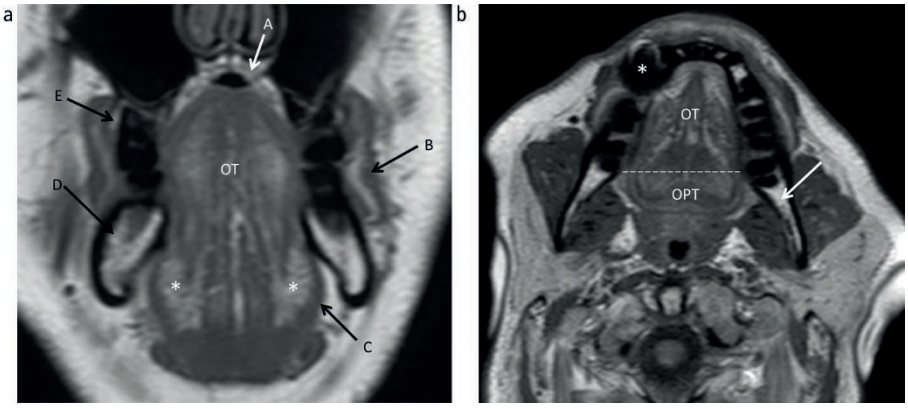

Fig. 1 Normal MRI anatomy of the oral cavity: (a) coronal and (b) axial T1-weighted images of the oral cavity. (a) Shows paired sublingual glands (*) in the sublingual spaces; (b) shows dental amalgam artefact (*) obscuring some local detail. The oropharyngeal tongue (OPT) is the posterior one third of the tongue behind the plane of the circumvallate papillae (not seen on MRI and approximated by dashed line). OT = oral tongue, OPT = oropharyngeal tongue, A = hard palate, B = buccinator muscle, C = mylohyoid muscle, D = mandibular alveolar bone, E = maxillary alveolar bone

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made clinically and with biopsy for histological analysis.

Although the oral cavity and neck can be easily examined by dentists patients often present with advanced disease. Most patients will see their doctor rather than their dentist if they have an oral problem that is not tooth related.[5]

This article aims to review the multimodality approach to imaging of oral cavity malignancy. In addition, it will also review the multidisciplinary approach to diagnosis and management of these tumours as multiple specialities are crucial for effective treatment.

Table 1 Summary of the eighth edition of the TNM classification for cancer of the oral cavity and lip. Reproduced with permission from Brierley J D, Gospodarowicz M K, Wittekind C (editors), TNM classification of malignant tumours, 8th edition, John Wiley & Sons Inc., 2017[18]

Primary tumour	
T1	Size ≤2 cm and depth of invasion ≤0.5 cm
T2	Size ≤2 cm and depth of invasion >0.5 but ≤1.0 cm
	or Size 2–4 cm, and depth of invasion ≤1.0 cm
T3	Size >4 cm or depth of invasion >1.0 cm
T4	Moderately advanced or very advanced disease
	T4a (oral cavity) tumour invades through the cortical bone of the mandible or maxillary sinus, or invades the skin of the face
	T4a (lip) tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin
	T4b (lip and oral cavity) tumour invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery
Cervical lymph nodes – clinical classification	
N0	No lymph node metastasis
N1	Metastasis in a single ipsilateral lymph node, ≤3 cm, without extranodal extension
N2a	Metastasis in a single ipsilateral lymph node, 3–6 cm, without extranodal extension
N2b	Metastasis in multiple ipsilateral lymph nodes, ≤6 cm, without extranodal extension
N2c	Metastasis in bilateral or contralateral lymph nodes, ≤6 cm, without extranodal extension
N3a	Metastasis in any lymph node >6 cm, without extranodal extension
N3b	Metastasis in any lymph node with clinical extranodal extension
Distance metastasis	
M0	No distant metastasis
M1	Distant metastasis

Table 2 Staging of oral cancer based on the TMN staging. Reproduced with permission from Brierley J D, Gospodarowicz M K, Wittekind C (editors), TNM classification of malignant tumours, 8th edition, John Wiley & Sons Inc., 2017[18]

	T stage	N stage	M stage
Stage 1	T1	N0	M0
Stage 2	T2	N0	M0
Stage 3	T3	N0	M0
	T1/T2/T3	N1	M0
Stage 4A	T4a	N0/N1	M0
	T1/T2/T3/T4a	N2	M0
Stage 4B	Any T	N3	M0
	T4b	Any N	M0
Stage 4C	Any T	Any N	M1

Staging

Cancer is staged using the TNM (tumour, lymph node, metastasis), where 'T' describes the extent of the primary tumour, 'N' refers to the absence/presence of lymph node involvement and 'M' refers to absence/presence of distance metastatic involvement.[6] Traditionally, primary tumour staging is dependent on tumour size, extent and presence of bone invasion. The latest version of the TNM classification is shown in (Table 1) and includes depth of invasion (DOI) of the primary tumour and the presence/absence of extranodal extension (ENE).[7] Depth of invasion of tongue tumours is significantly associated with increased risk of neck nodal disease and ENE is associated with poor local control and a poor prognosis.[8] A joint statement on the use of the latest TNM staging has been issued recently. This supports the latest TNM staging for the description of the anatomical extent of disease in head and neck cancer.[9] Survival rate is related to the stage of the disease (Table 2), so information from imaging is crucial in providing an indication of prognosis. For instance, the one-year and three-year survival rates for patients with early disease (stage one and two) is around 90% and 65% respectively but for late disease (stage three and four) drops to 80% and 45% respectively.[10] Imaging is also vital so that appropriate treatment can be planned. Treatment is aimed at clearing disease and preserving oral function and quality of life. Surgery is the treatment of choice for early stage cancer[11] and brachytherapy (placement of radioactive implants into the cancer) is also an option. Late stage cancer management includes surgery and reconstruction, radiotherapy and chemotherapy.[3]

Imaging

Imaging is primarily used in staging the disease. The Royal College of Radiologists UK recommend the following imaging modalities in the staging of oral cancer:[12]

- Magnetic resonance imaging (MRI)
- Computed tomography (CT)
- Positron emission tomography-computed tomography (PET-CT)
- Ultrasound.

Dental amalgam artefacts can degrade images of the oral cavity on CT and MRI

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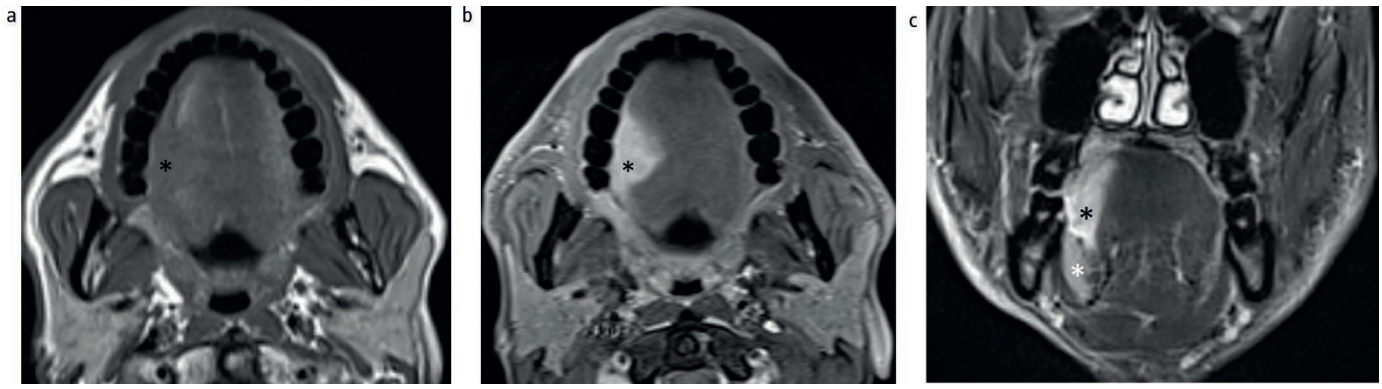

Fig. 2 MRI of oral tongue SCC. (a) axial T1-weighted image shows tumour as isointense lesion (black *) which becomes more conspicuous (black *) on the axial fat-supressed post-gadolinium enhanced T1-weighted image (b). (c) Coronal STIR image shows high signal tumour (black *) at the right lateral aspect of the tongue abutting inferiorly at the right sublingual gland (white *) in the floor of the mouth

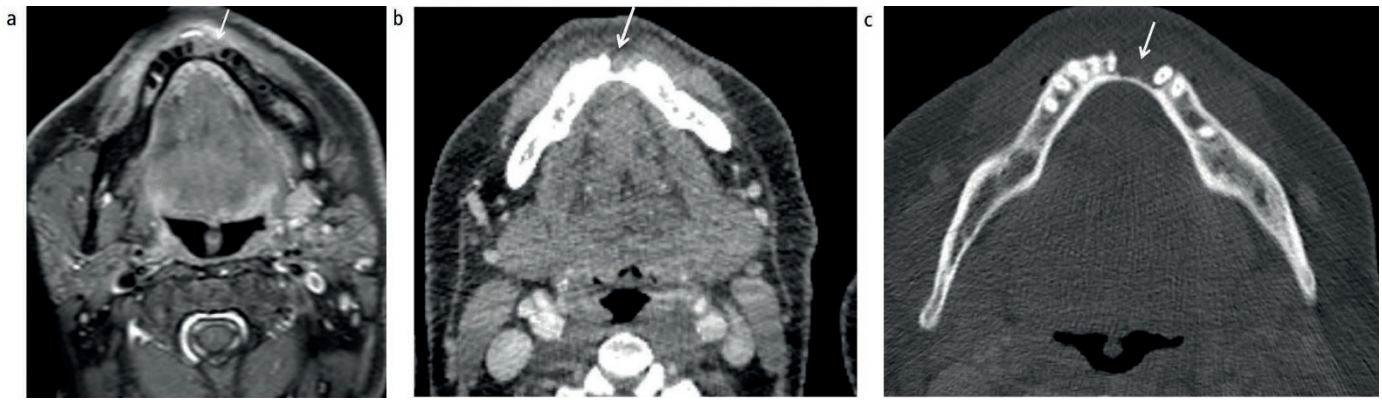

Fig. 3 MRI and CT of anterior mandible gingival SCC. (a) Axial post-gadolinium enhanced fat-suppressed T1-weighted image shows enhancing lesion (arrow) invading into the medullary cavity of mandible alveolar bone. The lesion is also depicted than on the axial contrast enhanced CT image (b). (c) High resolution bone-weighted CT depicts well the bony cortical destruction and erosion (arrow)

(Fig. 1b) and obscure necessary detail for primary tumour staging. Following biopsy, a small lesion may be removed completely, a lesion may appear substantially smaller on imaging or conversely appear larger with added post-biopsy oedematous changes.

Magnetic resonance imaging

MRI does not use ionising radiation. The patient lies on a table inside the machine and is placed in a strong magnetic field. This causes the free protons within the patient's tissues to align with the magnetic field. A series of radio frequency pulses are then sent into the patient which alter the magnetic field of the protons. When pulses are switched off, the protons start to align with the magnet again. As they do so a signal is produced, from which a picture can be reconstructed. The type of image produced is dependent upon the sequence of the pulses sent into the patient. Paramagnetic contrast agents based on gadolinium are used with some sequences to improve the contrast of the images.

Typical sequences include:

T1 weighted: with and without contrast to show the primary tumour (Figs 2a and 2b). Post contrast images require fat suppression for better depiction of the disease within the oral cavity and neck. Tumours generally enhance with the use of contrast, making identification of the extent of the tumour easier (Fig. 2b). Pathological nodes can also be identified.

T2 weighted: demonstrates disease as a high (bright) signal. As a consequence, a T2 weighted scan may be used to visualise the primary tumour and pathological lymph nodes.

Short tau inversion recovery (STIR): this sequence suppresses the signal from fat and also shows disease as a high (bright) signal against a dark fat background (Fig. 2c). This used to identify the extent of the primary tumour in the assessment of pathological lymph nodes.

MRI has better soft-tissue resolution than CT. MRI is also better than CT at demonstrating bone marrow involvement and perineural spread and is regarded as the preferred imaging modality for staging oral cancer.[13] In many cases though, CT and MRI investigations are complementary (Figs 3a, 3b and 3c). Serial MRI with post-treatment baseline scans is also used in many centres to detect recurrent disease, especially in the deeper neck regions which are not easily examined clinically (Fig. 4a). There are various benefits for each of these modalities depending on the specific circumstances (Table 3). A further development is diffusion-weighted imaging (DWI) which is an MRI technique that may have value in predicting the likely response to chemoradiation treatment and in the detection of tumour recurrence following treatment.[14,15]

Computed tomography

CT is a scan that involves the use of ionising radiation. The patient lies on a table and is moved through the gantry aperture of the CT machine while the x-ray source and detectors rotate around the patient. This produces a helical dataset from which axial, coronal and sagittal images can be reconstructed. Iodinated

Table 3 Advantages and disadvantages of the main imaging modalities used in the assessment of oral cancer

Imaging modality	
MRI	Advantages No radiation dose Excellent contrast resolution Good for perineural spread and bone marrow involvement Deep lymph nodes can be assessed
	Disadvantages Long scan time Can be claustrophobic for some patients Movement artefact can degrade image Ferromagnetic restorations (such as stainless steel crowns) can cause significant artefacts by disturbing the magnetic field Cannot be used if patient has ferromagnetic foreign bodies.
CT	Advantages Quick to perform Excellent spatial resolution The use of iodinated contrast helps in identifying disease Deep lymph nodes can be assessed Good for imaging cortical bone involvement
	Disadvantages Radiation dose Possible allergy to iodinated contrast Dental amalgam can cause beam hardening artefact and star (metal) artefact significantly degrading the image Limited contrast resolution
PET CT	Advantages Very sensitive test for small malignancies Can demonstrate widespread disease in a single investigation.
	Disadvantages Access can be limited at some centres Expensive Radiation dose Care must be taken in interpreting images as FDG is also taken up by normal tissues Misregistration of the PET and the CT can make interpretation difficult
US	Advantages Inexpensive Quick, easy to complete Biopsy of suspicious nodes can be carried out at the same time
	Disadvantages Hard tissue assessment not possible Deep lymph nodes cannot be assessed (retropharyngeal, retrotracheal and mediastinal groups) Structures deep to the mandible are difficult to visualise due to the shielding effect of the jaw Very operator dependent

contrast is generally injected just before the scan to increase the diagnostic yield. The data from a single scan can be used to reconstruct images on both soft tissue and bony windows.

In general, MRI has superseded CT for primary tumour and nodal staging. Subject to scanner availability and radiologist preference, there are centres in the UK which use CT routinely, though the soft tissue resolution is better with MRI.

However, there is still a definite role for CT in staging. Once malignancy has been confirmed, CT body staging is recommended to assess for distant metastases. The specific protocol will vary from centre to centre. Many centres limit the CT staging to the thorax to assess for lung metastases.

There may also be a role for CT within the head and neck in addition to MRI. CT is particularly good at demonstrating cortical bone invasion (Fig. 3c). Therefore, in oral cavity malignancy, subtle encroachment into the mandibular or maxillary cortex may be assessed with high resolution CT. In a practical approach, a non-contrast CT of the maxilla or mandible can be performed at the same time as the staging CT thorax or CT body.

Cone beam CT has been suggested in the detection of mandibular invasion as it is slightly more sensitive than conventional CT, but further studies need to be undertaken before it can be recommended routinely.[16]

Positron emission tomography-computed tomography

For this investigation a radioisotope such as 18F-fluorodeoxyglucose (18FDG) is injected into the blood stream. The 18FGD is a glucose analogue and gets taken up preferentially by cancer cells. The 18FGD decays producing positrons which are detected by a gamma camera. The areas of increased activity are co-registered with the CT scan so the cancerous tissues may be identified. This examination carries with it a much higher radiation dose than CT and therefore its use needs to be particularly justified. Interpretation may be difficult as 18FGD is also be taken up by normal tissues such as the intrinsic tongue muscles and in inflammatory conditions such as dental abscesses.

PET-CT is mainly indicated for detecting and staging recurrent or post-treatment disease (Fig. 4b). For primary disease, PET-CT is recommended in patients with advanced stage oral cavity cancer as there is a higher risk of metastatic and distant spread. Generally, PET-CT is also recommended in those patients who present with a metastatic lymph node, with an unknown primary tumour.

Ultrasound

Ultrasound is an excellent imaging modality used in the assessment of the cervical lymph nodes. The ultrasound probe contains a transducer which sends ultrasound waves into the neck tissues. Any sound waves that are 'reflected back' are picked up by the same transducer and used to create an image on the screen. A coupling gel is placed between the probe and the skin surface to ensure a good contact. This is required so the sound waves will propagate into the tissues.

The operator moves the probe over the neck in a systematic fashion examining the lymph nodes for any signs of malignancy. Enlarged, rounded, hypoechoic (dark) nodes lacking

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a hilum (Fig. 5a) with a chaotic blood flow (on colour Doppler) are highly suspicious for malignancy. Needle sampling of any suspicious nodes can also be carried out under ultrasound guidance.

High resolution intraoral ultrasound with a small 'hockey-stick probe' can be used to assess tumours where accessible in the oral cavity (Fig. 5b). It can be used to depict tumour size and depth of invasion[17] and is particularly helpful with small tumours which are not particularly well depicted on MRI or CT. As the new TNM classification includes depth of invasion of the tumour, ultrasound may have an increasing role in the staging of the primary tumour, particularly T1 and T2 disease.

Other radiological investigations

Panoramic radiography will show gross bony involvement by a malignant tumour (Fig. 6) and may be useful in planning resection and reconstruction planning.[12] The panoramic radiograph is often requested to make a dental assessment before radiotherapy. Periapical radiographs are more accurate in detecting caries and periapical disease than panoramic radiographs so these should be used whenever possible. It is important that the appropriate dental treatment is performed before radiotherapy to help prevent osteoradionecrosis.

The doses from various investigations used in the management of oral cancer are shown in Table 4.

Multidisciplinary approach and pathways

Due to the anatomical location, oral cavity malignancy is one of the few cancers that may present to a general dental practitioner as well as the general medical practitioner. Referrals of oral cavity lesions from dentists or general practitioners suspicious of malignancy will then be fast tracked via local guidelines to an oral and maxillofacial unit. From here, they will undergo a series of investigations including the aforementioned radiological investigations. Histopathology is key and obtaining this will vary on a case by case basis. Examples include:

- Incisional biopsy of the primary lesion under local anaesthetic in the clinic
- Incisional biopsy of the primary lesion under general anaesthetic if the lesion is difficult to access
- Fine needle aspiration or core biopsy of a palpable suspicious (metastatic) lymph node in the clinic setting

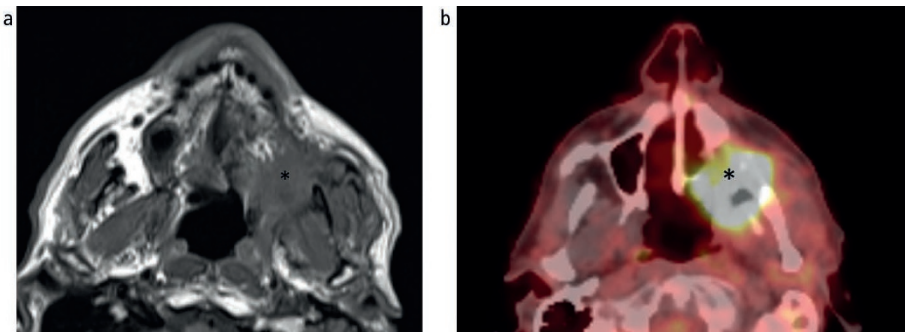

Fig. 4 Recurrent oral cavity tumour. (a) Axial T1-weighted MRI image shows intermediate signal soft-tissue lesion at the left retromolar trigone and pterygomandibular raphe in keeping with recurrent disease (*). This demonstrates significant uptake of tracer on the PET-CT scan (b)

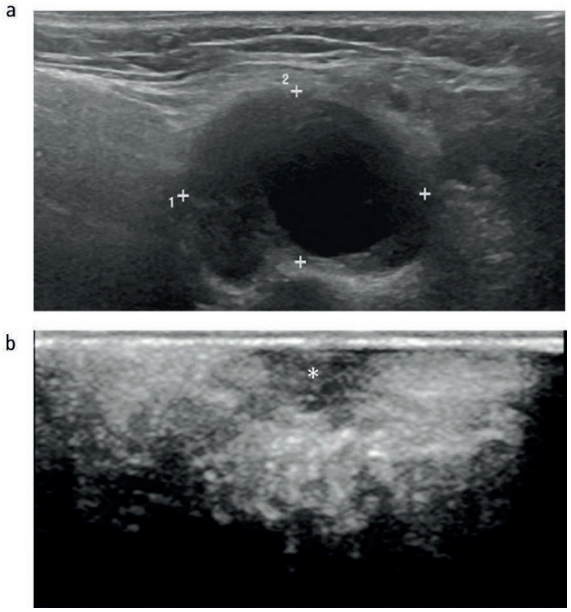

Fig. 5 Use of ultrasound. (a) Ultrasound image of an enlarged neck node shows abnormal features with central necrosis and loss of normal fatty hilum. (b) Intra-oral ultrasound image depicts well a small tongue SCC (*) as a hypoechoic lesion. Size measurement and depth of invasion can be obtained

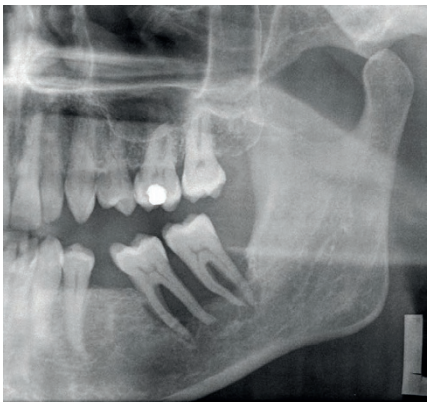

Fig. 6 Panoramic radiograph showing irregular radiolucent lesion involving the lower left molars due to oral malignancy

- Fine needle aspiration or core biopsy of a radiologically suspicious impalpable node referred to radiology performed under ultrasound guidance.

Once the radiological and histopathological reports are available, the patient will then be discussed in the multidisciplinary meeting (MDM). This will call on the joint expertise of oral maxillofacial surgeons, oncologists, histopathologists and radiologists among other medical specialities. In particular, ear nose and throat (ENT) head & neck surgeons will naturally be a part of the head & neck oncology MDM and will offer their expertise particularly with reference to malignant encroachment into adjacent subsites such as maxillary sinuses or pharynx. While oral maxillofacial surgeons in general are adept at neck dissection for nodal disease, an ENT opinion is valuable or even a joint surgical case may be performed depending on local expertise.

There are multiple other disciplines as part of the MDM. These include specialist nurses, speech language therapists, dieticians and possibly restorative dentists dependant on local practice.

Summary

Earlier diagnosis of oral cavity malignancies, as with other subsite malignancies, will help with prognosis. Diagnosis and management of oral cavity malignancy benefits greatly from a multimodality and multidisciplinary approach.

Table 4 Effective doses from the main radiological investigations used in the investigations of patients with oral cancer

Investigation	Effective dose
CT neck	3.2 mSv[19]
CT chest	6.7 mSv[19]
Whole body PET-CT	14 mSv[20]
Panoramic radiograph	0.0003-0.022 mSv[21]
Periapical radiograph	0.0027–0.038 mSv[21]

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