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Foreword

The first edition of *Imaging in Oncology* was published in 1998 at a time when radiologists began to play an increasingly pivotal role within a multidisciplinary team, planning the management of patients with cancer together with medical and clinical oncologists, surgeons, and pathologists. The aim of the first and subsequent editions was to familiarize its readers with the optimal use of state-of-the-art imaging and to maximize the efficacy of its application dependant on factors such as tumour type, mode of spread, patterns of recurrence, and developments in therapy.

Since publication of the first edition over twenty years ago, there have been spectacular advances in imaging technology, matched by better understanding of tumour behaviour and major advances in cancer therapy, all of which have led to improved patient outcomes. Such advances continue to shape and develop modern approaches to cancer management, so that today radiologists working in cancer imaging face ever changing challenges in maintaining an effective central role within the multidisciplinary team. The purpose of this new edition of *Imaging in Oncology* is to provide an up to date leading edge approach to cancer imaging, thereby contributing to the ability of the radiologist to meet these challenges effectively.

The new editors, Dr Anju Sahdev and Dr Sarah Vinnicombe, are both internationally recognized and highly experienced oncological radiologists. They have identified these challenges and have recruited a team of outstanding contributors, who include many internationally acclaimed clinical scientists and academics. Through their careful editing, Drs Sahdev and Vinnicombe have built effectively on previous editions, maintaining the aims and editorial policy of earlier texts, while introducing new and innovative improvements.

The sections covered in over 800 pages of this book include the essential components required for the practice of oncological radiology: staging the primary tumour, the detection of metastases, evaluating the response to treatment, and the effect of treatment on normal tissues. The increasingly important application of molecular and functional techniques to the evaluation of patients with cancer is dealt with admirably.

This comprehensive text is the product of the hard work of the two dedicated editors, who have ensured a continuity of style, content, and purpose throughout the book. Within its pages a new generation of radiologists will surely find the answers to their questions and guidance on optimizing their practice of oncological imaging.

Professor Rodney Reznek, MBChB, MA, PhD, FRCP, FRCR
Professor Dame Janet Husband, DBE, FMedSci, FRCP, FRCR
**Preface**

*Imaging in Oncology* has a distinguished history and was first conceived as a comprehensive text promising the reader a clinical understanding of various cancers, their behaviour, and imaging features. Since then each edition has matched the success of the first, so when we were approached by Professors Husband and Reznek it was both a privilege and a formidable undertaking to develop the fourth edition.

As a speciality, Radiology has ever-increasing complexity and subspecialization and this necessitated the inclusion of new and relevant updates, particularly in PET CT and new technologies in MRI and CT. Needless to say, this was comprehensively captured par excellence by the authors, who are internationally renowned experts in their subjects. Each chapter includes clinically pertinent details and discussion of imaging modalities and their applications. The advantages and limitations of each modality are discussed intelligently by the authors in relation to clinical parameters that affect patient management. We are extremely grateful to the authors for their dedication and expertise, which they offered so graciously.

In this edition we have endeavoured to retain the main strengths of the previous editions - the beautiful illustrations, excellent tables, and synopsis key points. In contrast to the previous editions, the full lists of references for each chapter have been placed on-line, to maximize the authors’ text: they may be found as Support Material on the book’s page on the CRC Press website (https://www.crcpress.com). Chapters on primary tumours of the central nervous system, paediatric oncology, and malignancy in the immunocompromised host have been omitted, as these are better served by their specialist dedicated texts. On the other hand, there are new chapters on applications of immunotherapy and targeted therapies, immunotherapy response assessment, and tumour-specific response criteria. With these updates, we believe the book remains readily comprehensible, succinct, authoritative, and importantly as pertinent to modern oncological imaging as the landmark first edition.

As editors, ours has been a pleasurable journey, through which we have gained new insights and understanding of the subspecialties and we trust this fourth edition of *Imaging in Oncology* brings the reader the same satisfaction and learning.

Dr Anju Sahdev, MB MS, MRCP, FRCR
Dr Sarah J Vinnicombe, BSc MB BS, MRCP, FRCR
Acknowledgements

The editors and publisher wish to acknowledge all those authors who have contributed to previous editions of Imaging in Oncology, particularly those who authored chapters in the 3rd edition but have not been able to participate in the preparation of the fourth edition who we list below.

We are indebted to Dee Maclean for her beautiful artwork which has been an outstanding feature of Imaging in Oncology throughout all of its four editions and also to Maureen Watts, Julie Jessop, and Janet Macdonald whose work on the text and images in previous editions is replicated in this new fourth edition.

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INTRODUCTION
Computed tomography (CT) or magnetic resonance imaging (MRI) of the head and neck is frequently performed to evaluate most primary head and neck cancers. Most are mucosal and the mucosal extent can be evaluated best by visual inspection by the clinician. However, these tumours have the tendency to spread submucosally, and this extension into the deeper tissue planes may be impossible to detect by clinical examination. Some regions such as the base of the skull, pterygopalatine and infratemporal fossa, orbits, and brain are beyond clinical evaluation, although critical management decisions have to be made based on the involvement of these structures; imaging findings are of the utmost importance in such cases. Perineural and/or perivascular spread, leading to tumour progression, local or distant recurrences can be detected by imaging. Bone involvement, or cartilage invasion or destruction, can be visualized using CT or MRI. Metastatic adenopathies can be identified, sometimes still in a subclinical stage or in sites inaccessible by clinical examination, such as in the retropharyngeal or paratracheal lymph nodes. All of these findings can profoundly influence the staging and management of the patient with head and neck cancer. Finally, imaging may be used to monitor tumour response and to detect recurrent or persistent disease before it becomes clinically evident, possibly with a better chance for successful salvage. Besides imaging findings, the results of initial pathological specimens and smoking history are vital for patient management, and these patients should be formally staged in a multidisciplinary setting.

NORMAL ANATOMY
Oral cavity
The oral cavity comprises the mucosal surface of the lips, the anterior two-thirds of the tongue (demarcated by the circumvallate papillae), the floor of mouth including sublingual spaces, the buccal mucosa which lines the cheeks, the gingiva (mucosa overlying upper and lower alveolar ridges of the maxilla and the mandible, respectively), the hard palate, and the retromolar trigone (Figure 1.1). The gap between the cheek and the alveolar ridges, which can be distended by air when puffing the cheeks, is termed the oral vestibule.

The oral tongue includes the tip, the ventral surface (undersurface), the dorsal surface, and the two lateral borders. The tongue muscles are subdivided into intrinsic or extrinsic groups, with the latter having external bony attachments. Each half of tongue receives a separate blood supply and innervation, and they are united by an avascular fibrofatty midline raphe (lingual septum). The root of the tongue comprises the genial muscles and the septum below the floor of the mouth mucosa.

The floor of the mouth is located beneath the mobile tongue and is enclosed by the lower alveolar ridges. Its inferior boundary includes the sheet-like mylohyoid muscle, separating the floor of the mouth from the submental space below. Its contents are within the sublingual spaces, which include the sublingual and minor salivary glands, the submandibular duct (Wharton duct), and a part of the hyoglossus muscle, as well as the lingual artery, vein, and lingual and hypoglossal nerves. The vessels and nerves are often termed the lingual neurovascular bundle.

The retromolar trigone is a triangular-shaped mucosa behind the last lower molar tooth and extending over the anterior margin of the ramus.

Pharynx
The pharynx is divided into three sections: the nasopharynx lies behind the nasal cavity, the oropharynx lies behind the oral cavity, and the hypopharynx lies behind the larynx. The hypopharynx merges with the oesophagus at the lower level of the cricoid cartilage (Figure 1.2).

The outer muscular wall of the pharynx is formed by the overlapping superior, middle, and inferior pharyngeal constrictor muscles, which are enclosed by fascia (buccopharyngeal fascia). The superior constrictor muscle attaches to the skull base via an aponeurosis termed the pharyngobasilar fascia. The superior constrictor muscle is attached anteriorly to the buccinator muscle via a ligamentous band termed the pterygomandibular raphe, which extends vertically between the skull base and the mandible.

The anatomy of the nasopharynx is described in the section “Nasopharyngeal tumours”.

The oropharynx is divided into four regions: the posterior third of the tongue (or tongue base) and two valleculae, the soft palate, the posterior wall, and the two lateral walls. Posterior to the muscles of the tongue base, there is a variable amount of lymphoid tissue termed the lingual tonsil. The valleculae are shallow depressions behind the tongue base and anterior to the epiglottis, which are bordered medially and laterally by the median and lateral glossoepiglottic folds, respectively (Figure 1.2).
**Figure 1.1** The subsites of the oral cavity.

**Figure 1.2** Normal upper aerodigestive tract. (a) Sagittal and (b) coronal drawing of the upper aerodigestive tract illustrates its major subdivisions: the nasopharynx (N), oropharynx (OP), oral cavity (OC), hypopharynx (HP), and larynx (L); and structures.
The lateral walls of the oropharynx contain vertical ridges termed anterior and posterior tonsillar pillars, formed by palatoglossus and palatopharyngeus muscles, respectively. Between these pillars is lymphoid tissue termed the faucial or palatine tonsil.

The hypopharynx extends from the level of the hyoid to the lower border of the cricoid cartilage. Hypopharyngeal subsites include the postcricoid region (which overlies the posterior cricoid arch), the posterior wall, and two piriform sinuses. The piriform sinuses are anterolateral recesses shaped like inverted pyramids; the anteromedial wall is the aryepiglottic fold; and the lateral wall comprises parts of the thyrohyoid membrane, thyroid cartilage, and inferior constrictor muscle (the posterior wall is open).

Lymphoid tissue within the pharynx (lingual, palatine, and nasopharyngeal tonsils) is collectively termed Waldeyer’s ring. Although prominent between infancy and adolescence, this usually regresses by adulthood but may persist or enlarge because of recurrent infections, inflammatory conditions, and lymphomatous infiltration. Reactively enlarged tonsils often appear striped on imaging reflecting normal crypt architecture. Small pockets of air, mucous retention cysts, and focal calcifications termed tonsilloliths may also be present. Tonsils are normally symmetrical, although minor asymmetry of the faucial tonsils can be physiological. Any tonsillary asymmetry must be correlated clinically as this is an important feature of malignancy.

The neck is subdivided by fascia and other structures into spaces which can explain pathways of local tumour and infectious spread (Figure 1.3). This includes the oral cavity and pharynx within the pharyngeal mucosal space, which, at the level of the nasopharynx and upper oropharynx, is bordered laterally from front to back by the buccal space, the masticator space, the parapharyngeal space, and the carotid space (also referred to as post-styloid parapharyngeal space), and posteriorly by the retropharyngeal space, behind which is the perivertebral space. In the suprathyroid neck, each parapharyngeal space is a readily identifiable landmark on CT and MRI, appearing as a triangular-shaped region of fat (loose areolar tissue).

**Key points: Normal anatomy**

- The oral cavity and oro- and hyopharynx are further divided into anatomical subsites.
- After the age of 40, no significant amount of lymphatic tissue is expected to be present in the Waldeyer’s ring.
- Waldeyer’s ring is normally symmetrical apart from the faucial tonsils, which may be slightly asymmetrical, although this should be correlated clinically.
- The neck is subdivided into spaces that can explain pathways of local tumour spread.

**IMAGING MODALITIES**

**Conventional radiography**

Conventional radiography has limited use in detection of oral or pharyngeal tumours. Dental radiographs and barium swallows may disclose an advanced oral cancer or oropharyngeal or hypopharyngeal tumour but are
respectively. On T1W sequences post-gadolinium, tumours isointense and mildly hyperintense to muscle on T1-weighted (T1W) and T2-weighted (T2W) sequences, respectively. On T1W sequences post-gadolinium, tumours show mild to moderate enhancement, which is greater than muscle but usually slightly less than normal mucosa. Diffusion-weighted imaging (DWI) is a useful adjunct; tumours including SCC and lymphoma show restricted diffusion due to their high cellularity restricting water diffusion, appearing bright on DWI images and dark on apparent diffusion coefficient (ADC) maps. Areas of tumoural necrosis and cystic change can increase diffusion and should be excluded from ADC measurements.

Computed tomography

Contrast-enhanced CT (CECT) is widely used as the workhorse because of its wide availability, diagnostic quality in most situations, and the thorax and liver can be also imaged to detect synchronous lung cancers and metastases. CT is quick and, hence, is preferred for frail patients or those with irrigative tumours causing intractable swallowing. CT scans should be thin collimation (usually 0.625 mm) and have an adequate contrast injection protocol, which may include slow single bolus with imaging delay of around 100 seconds or a split bolus technique to enhance arteries optimally. Additional manoeuvres can be used including a modified Valsalva manoeuvre or buccal insufflation (blowing the cheeks) to distend the piriform sinuses and oral vestibule, respectively. Streak artefacts caused by dental amalgam and hardware are a major limitation of CT, although gantry tilting and patient repositioning can reposition artefacts away from regions of interest. Tumour enhancement on CECT is variable, although most squamous cell carcinomas (SCCs) are hypoattenuating compared with mucosa and hyperattenuating relative to muscle and fat. Nevertheless, tumours are frequently isoattenuating to lymphoid tissue such that small cancers in the lingual and palatine tonsils may be obscured. Even in the absence of a contrast difference of tumour from the surrounding mucosa, other imaging features including abnormal mucosal thickening, asymmetry between sides, and submucosal involvement are clues to the presence and extent of primary tumour.

Magnetic resonance technique

MRI has a superior contrast resolution to CT and is the preferred technique for oral and pharyngeal tumours in cooperative patients. MRI is particularly useful for assessing bone marrow invasion, including in the jaw and skull base, as well as perineural spread. Motion artefacts due to swallowing, coughing, and tongue movements are a major limitation, whereas dental amalgam or other hardware artefacts, which also degrade images, are usually less severe than on CT. A standard protocol includes spinecho or turbo spin-echo T2-weighted images (T2WI) and plain and gadolinium-enhanced T1-weighted images (T1WI), with and without fat saturation. Multiplanar MRI acquisitions are recommended using a slice thickness of 4 mm or less, a high-resolution matrix (512²), and as small field of view as possible while allowing for signal to noise considerations.

Most head and neck cancers, including SCC, are isointense and mildly hyperintense to muscle on T1-weighted (T1W) and T2-weighted (T2W) sequences, respectively. On T1W sequences post-gadolinium, tumours show mild to moderate enhancement, which is greater than muscle but usually slightly less than normal mucosa. Diffusion-weighted imaging (DWI) is a useful adjunct; tumours including SCC and lymphoma show restricted diffusion due to their high cellularity restricting water diffusion, appearing bright on DWI images and dark on apparent diffusion coefficient (ADC) maps. Areas of tumoural necrosis and cystic change can increase diffusion and should be excluded from ADC measurements.

Ultrasound

Neck ultrasound (US) is widely used in the work-up of patients with palpable neck masses, which includes metastatic adenopathy from head and neck cancer. US is not used routinely for primary tumour assessment in SCC, although experienced operators may detect and stage tumours including oral cancers using small footprint transducers placed intraorally. US is excellent for problem solving when combined with ultrasound-guided fine-needle aspiration cytology (FNAC), for example, in patients with known head and neck malignancy and equivocally involved nodes on conventional imaging. Most nodal groups are evaluable by US, although exceptions include deep intraparotid, retropharyngeal, and posterior paratracheal groups.

PET-CT

Positron emission tomography combined with CT (PET-CT) is performed widely using fluorine-18-labelled fluorodeoxyglucose (FDG) and the clinical utility of this tracer reflects high rate of glucose uptake in cancer cells and inflammatory tissues. Most head and neck cancers, including SCC, nasopharyngeal carcinoma (NPC), and lymphoma, are FDG avid; exceptions include some salivary and spindle cell malignancies. For SCC, PET-CT indications include detection of occult primary tumours in patients with metastatic cervical lymphadenopathy, staging of locoregionally advanced tumours where the risk for distant metastases is high, post-therapeutic response assessment, and detection of suspected recurrences. PET-CT has a central role in lymphoma staging, response assessment, and surveillance. False negatives on PET-CT reflect insufficiently concentrated metabolic activity of small or necrotic tumours, or tumours being concealed by physiological hypermetabolism of adjacent lymphoid tissue including in Waldeyer’s ring. False positives are mainly due to coexisting inflammation, which is an important limitation in the post-treatment setting, and asymmetric physiological activity in muscles and brown fat.

Post-biopsy changes

Incisional or excisional biopsies of suspected primary tumours produce transient inflammatory changes mimicking tumour on CT, MRI, and PET-CT. Accordingly, imaging should ideally be performed before, or at least 2 weeks after, undertaking biopsies, especially for small tumours where there is a greater risk of erroneous upstaging.
TUMOUR TYPES

Squamous cell carcinoma

Squamous cell carcinoma (SCC) is the commonest non-cutaneous head and neck malignancy. Head and neck SCCs (HNSCCs) have varied appearances including shallow plaques, ulcers, exophytic masses, or deeply infiltrative lesions. Tumour spread is predictable, following paths of least resistance, with muscle invasion early and bone or cartilage invasion late due to resistance of the periosteum and perichondrium. Perineural and perivascular invasion is also common and often clinically silent initially. Lymphatic spread of SCC to cervical lymph nodes is a hallmark; sites with rich lymphatic drainage such as the hypopharynx and tongue base have high rates of nodal metastases, and midline structures frequently involve midline and bilateral nodal groups. Haematogenous spread in SCC is uncommon and usually associated with locoregionally advanced disease. Up to 15% of SCCs are ‘non classical’ variants, which vary in their appearance and aggressiveness (4).

Lymphoma (see Chapter 25)

Lymphoma accounts for 5% of head and neck malignancies and is usually non-Hodgkin type, which mostly affects the middle aged and elderly. About 11% of all non-Hodgkin lymphomas present with neck disease, and 50% of patients with neck disease also have systemic disease. Non-Hodgkin lymphoma can involve virtually any site in the neck; nodal involvement is most common, although extranodal localizations are also frequent. In the extracranial head and neck, two distinct extranodal sites are recognized: extranodal lymphatic localizations or involvement of Waldeyer’s ring and extranodal extralymphatic localizations (5). Hodgkin lymphoma is uncommon in the neck and almost invariably nodal disease (6).

Other malignancies

Under 5% of oral and pharyngeal tumours arise from minor salivary glands, of which over 50% are malignant. The hard palate is the commonest site involved (65%) (7). In terms of incidence, the majority are adenoid cystic carcinomas, mucoepidermoid carcinomas, or low-grade adenocarcinomas. Adenoid cystic carcinomas are high-grade tumours presenting in mid to late adulthood and are locally aggressive, often with a slow but relentless biologic course, a predilection for perineural spread, local recurrences, and distant metastases that may arise many years later (8). Mucoepidermoid carcinoma affects all ages and is the commonest salivary malignancy in children. It is classified into three histological grades with variable rates of recurrence and metastases (8).

Head and neck sarcomas are rare and are either spontaneous or radiation induced, the latter typically presenting years later in the irradiated field of a previous head and neck carcinoma. They are histologically varied; examples include rhabdomyosarcomas (under 1% of solid malignancies in adults but the third commonest extracranial malignancy in children and adolescents), osteosarcomas, and chondrosarcomas, the latter mostly affecting the maxillofacial skeleton and skull base, respectively. Sarcomas may be suspected due to clinical-radiological features differing from conventional head and neck SCC. Nasopharyngeal carcinoma is discussed in detail separately with reference to the nasopharynx. Other pathologies including malignant melanoma and metastases may rarely occur in the oral cavity and pharynx.

Epidemiology of oral cavity and pharyngeal squamous cell carcinoma

Head and neck cancer is the ninth commonest cancer worldwide, although there is geographical variation due to environmental and genetic factors (9). Globally, lip, oral cavity, and pharyngeal cancers accounted for approximately 530,000 new cancer cases and 230,000 deaths in 2012, representing 3.8% of all cancer cases and 3.6% of cancer deaths. The age-adjusted incidence for men is between 0.4 and 1.4:100,000/year, and it is 2–4 times lower in women. In Western Europe, about one-quarter each of head and neck cancers arise in the larynx, oral cavity, and pharynx, with the remainder in the thyroid gland, salivary glands, and other sites. In India, oral cancer is the commonest cancer of any type. SCC typically affects middle-aged persons, with a rising incidence up to the age of 70–80 years, although the incidence is rising in younger adults because of shifts in risk factor exposure. Prognosis is dependent on site and stage, equating to 65% at 5 years for the oropharynx compared with 28% for the hypopharynx (10).

Tobacco and alcohol are the main causative agents for oral and pharyngeal SCC; both are independently carcinogenic, although tobacco, whether smoked, chewed, or taken as snuff, is more potent. When combined, their effects are synergistic, increasing the relative risk by over 15 times (11). Oral chewing of betel quid with or without tobacco, which is a cultural pastime in parts of Asia, is also carcinogenic (11). All of these agents contain carcinogenic compounds capable of inducing genetic and epigenetic mucosal alterations, producing a wide field of premalignant changes that are invisible clinically. This process, termed ‘field cancerization’, explains why head and neck cancer patients may develop synchronous and metachronous cancers throughout the upper digestive tract (12). Gender differences in tobacco and alcohol usage explain the higher
incidence of SCC in men, as well as the recent rising incidence of oral SCC in younger women (11,13,14).

In the last few decades, human papilloma virus (HPV) has emerged as a carcinogenic agent for head and neck SCC (15,16). HPV has a tropism for oropharyngeal mucosa, especially the lingual and palatine tonsils, where its causal role for SCC is recognized (11). There are over 100 subtypes of HPV, of which several are implicated in HPV-driven oropharyngeal SCC (OPSCC), although HPV16 accounts for the majority (90%–95%) (11,16). HPV-related OPSCC is fundamentally different from HPV-negative OPSCC on a molecular level and occurs in younger individuals who often have no or limited tobacco or alcohol exposure. Importantly, HPV-driven OPSCC has greater treatment responsiveness and better prognosis than HPV-negative OPSCC, 65% vs. 28% survival at 5 years, respectively, although survival benefits fall in heavy smokers (16,17).

In the last few decades, there has been a progressive rise in OPSCC associated with HPV, particularly in developed countries, raising concerns regarding an incipient cancer epidemic; presently, in Europe and the US, approximately 70% of OPSCCs are HPV positive (11,18). There is some evidence linking this rise to sexual activity (19). The impact of existing or future HPV vaccination programs on this epidemic; presently, in Europe and the US, approximately 70% of OPSCCs are HPV positive (11,18). There is some evidence linking this rise to sexual activity (19). The impact of existing or future HPV vaccination programs on this cancer is currently unclear (20).

Other risk factors for head and neck cancer include poor oral hygiene, ultraviolet radiation (lip cancer), dietary insufficiencies, processed meat consumption and nitrosamine-rich foods, and specific occupational exposures (21–24). A minority of cancers are associated with rare heritable conditions or acquired immunodeficiencies (19).

### Key points: Tumour types and HNSCC epidemiology

- Squamous cell carcinoma is the most common head and neck malignancy, which is commonly associated with muscle invasion, perineural and perivascular spread, and lymph node metastases.
- The incidence of HNSCC is strongly linked to tobacco, alcohol, and betel quid consumption and HPV.
- There is a progressive rise in HPV-driven oropharyngeal SCC, especially in developing countries.
- HPV-positive OPSCC is molecularly fundamentally different from HPV-negative oropharyngeal SCC and has a better prognosis.
- Other malignancies including minor salivary tumours, lymphoma, and sarcomas represent a small but significant minority.

### ORAL AND PHARYNGEAL TUMOURS

#### Clinical presentation

Over 90% of oral cavity tumours are SCCs, with the remainder representing minor salivary tumours, lymphoma, melanoma, sarcomas, odontogenic tumours, and miscellaneous tumours. Symptoms include pain, bleeding, a lump, ulcer, dysphagia, trismus, loosening of teeth, and neck swelling due to nodal metastases. Rarely, a cancer in the floor of the mouth may present with submandibular swelling due to invasion of Wharton’s duct, or a palatal cancer may present with referred pain due to perineural spread to the skull base. Most oral cancers are detected at an early local stage because of pain interfering with chewing and swallowing and because this site is easy to inspect clinically, although a substantial proportion of patients still present with advanced disease. Involvement of different oral subsites varies geographically. In the West, the lip is the commonest site (~40%), partly due to ultraviolet exposure, followed by gingival and buccal mucosa (20%), oral tongue (15%), floor of mouth (15%), and hard palate (5%) (25). In Asia, the buccogingival region is the commonest site (73%), partly due to high rates of betel quid and tobacco chewing (26).

#### Staging and radiological features

The T staging is based on tumour location, size, and involvement of specific structures (Table 1.1). Depth of invasion is a new staging criterion included in the eighth edition of TNM staging as it is a strong predictor of nodal metastases (27) and is defined pathologically as the position of the deepest point of invasion relative to the basement membrane of the closest adjacent normal mucosa. Tumour thickness on imaging correlates with the depth of invasion, although these terms are not interchangeable, especially as tumour thickness potentially may overestimate or underestimate depth of invasion if tumours are exophytic or ulcerated, respectively (28). Tumours of the cutaneous lip (hair-bearing portion) have a similar prognosis to other cutaneous SCCs and are staged under a new group termed ‘cutaneous carcinomas of the head and neck’ (TNM not shown) (29).

#### Table 1.1 T staging of squamous cell carcinoma of the lip and oral cavity

<table>
<thead>
<tr>
<th>T stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>Carcinoma in situ</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour ≤2 cm in greatest dimension and DOI ≤5 mm</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour ≤2 cm and DOI &gt;5 mm but ≤10 mm or Tumour &gt;2 cm but ≤4 cm and DOI ≤10 mm</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour &gt;4 cm or &gt;10 mm DOI</td>
</tr>
<tr>
<td>T4a</td>
<td>Lip: Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (of the chin or nose)</td>
</tr>
<tr>
<td>• Oral cavity: Tumour invades through cortical bone of the mandible or maxilla, maxillary sinus, or invades the skin of face*</td>
<td></td>
</tr>
<tr>
<td>T4b</td>
<td>Lip and oral cavity: Tumour invades masticator space, pterygoid plates, skull base or encases internal carotid artery</td>
</tr>
</tbody>
</table>

*Superficial erosion of bone/tooth socket by gingival primary cancer is not sufficient to classify as T4

Source: Adapted from Brierly JD et al. (2017).

Note: DOI = depth of invasion
Lip
Approximately 90% of lip cancers arise in the lower lip, 7% in the upper lip, and 3% in the commissures. Most are SCCs, followed by basal cell carcinomas. Early cancers are staged clinically. CT and/or MRI are required for advanced cancers, which can invade the adjacent skin, nose, mandible, maxilla, floor of mouth, and root of tongue and can spread perineurally along the mental nerves.

Buccal mucosa, gingiva, and retromolar trigone
Most cancers involving cheek mucosa originate near the teeth occlusal line and are clinically apparent. Invasion of the overlying buccinator muscle occurs early, and from here, tumours can readily invade the buccal fat, subcutaneous tissues, and skin. Superficial spread along the buccogingival sulci onto the alveolar gingiva and posteriorly to the retromolar trigone is also common; detecting this spread is assisted on CT using buccal insufflation.

Most gingival cancers arise along the lower jaw due to pooling of saliva, which concentrates carcinogenic agents in the dependent areas. Tumours can spread superficially, crossing the lingual (medial) and buccal (lateral) buccogingival sulci onto the cheek and floor of the mouth. Deeper infiltration, including bone invasion, is also common, initially manifesting as cortical erosions, followed by cancellous bone destruction and/or marrow infiltration; accordingly, CT and MRI may be required for accurate staging. Of importance, superficial erosion of bone or a tooth socket by tumour without deeper bone involvement does not influence prognosis and, hence, T stage. MRI is highly sensitive for marrow involvement but not as specific as reactive marrow changes can mimic tumour. For tumours invading the mandible, perineural spread along the inferior alveolar nerve towards the skull base should be excluded. Upper buccogingival sulcus cancers may invade through the upper alveolus into the maxillary sinus (Figures 1.4 and 1.5).

Figure 1.4 Coronal gadolinium-enhanced, T1W spin-echo MRI image in a patient with an upper gingivobuccal sulcus cancer (white asterisk). The lesion extends into the buccinator space (black arrowheads) and erodes the alveolar process of the maxilla (white arrowhead); the maxillary sinus is also invaded (black asterisks).

Figure 1.5 Coronal and axial post-contrast image CT images with buccal insufflation. (a) Coronal image shows an extensive left oral cavity cancer involving left buccal mucosa (black arrow) and upper buccogingival sulcus, extending medially along the upper alveolus, which is partially eroded, and onto the left hard palate (white arrow). There is also focal invasion into the maxillary sinus (dashed white arrow). (b) Axial image showing the tumour reaching the left retromolar trigone (asterisk). On both planes, there is gross invasion through the buccinator muscle into the buccal fat (black arrows). Buccal insufflation allows the mucosal extent of tumours in the vestibule to be better assessed. See the normal mucosa along the right vestibule (Figure 1.5a), including retromolar trigone (black arrowhead).
Tumours of the oral cavity and pharynx

Retromolar trigone SCC spreads readily between the oral and oropharyngeal subsites, particularly the tongue base, tonsil, palate, buccal mucosa, gingiva, and floor of the mouth. Mandibular invasion can occur with even relatively small tumours and thus should be actively excluded by cross-sectional imaging. Extramucosal invasion can involve the cheek (buccinator space), medial pterygoid muscle (masticator space), or mandibular body and ramus and can spread via the pterygomandibular raphe to the skull base (Figure 1.6).

Oral tongue

Most tongue cancers originate in the ventral or lateral tongue and grow both superficially as well as infiltrate deeply. Extension into the floor of mouth is common, and from here the lower gingiva and mandible may also be involved. Cancers along the mid third may extend posteriorly into the oropharyngeal tongue. Tumour thickness perpendicular to the mucosal surface should be documented as this, combined with clinical examination, predicts depth of invasion pathologically and hence is used for T staging clinically. The closest distance of tumour to the lingual neurovascular bundles and the midline raphe should also be documented as these influence feasibility and type of surgical resection possible. For all but the smallest cancers, cross-sectional imaging is essential for accurate staging (Figure 1.7).

Figure 1.6 Axial CECT images in a patient with an extensive cancer centred on the right retromolar trigone. (a) From the region of the retromolar trigone (black asterisk), the soft tissue mass extends towards the medial pterygoid muscle and anterior tonsillar pillar (black arrows). Extension towards the base of the tongue and floor of the mouth (white arrowhead) is seen. The lesion causes mandibular osteolysis and grows massively in the soft tissue of the cheek (white arrowheads). (b) The tumour extends cranially along the anterior margin of the mandibular ramus and into the soft palate (asterisks; medial tumour border in soft palate indicated by black arrowhead); superior extension is also seen underneath the buccinator muscle (white arrowheads). (c) The lesion reaches lateral to the maxillary alveolar process (white arrowheads) and maxillary tubercle (black arrow); also at this level, tumour involvement of the palate is recognized (white arrows).

Figure 1.7 (a) Axial gadolinium-enhanced, T1W spin-echo MRI. Enhancing soft tissue mass in the right side of the oral tongue confirmed as squamous cell carcinoma. It crosses the midline (arrowheads) and extends posteriorly to the tongue base (arrow). (b) Coronal gadolinium-enhanced, T1W spin-echo MRI. Inferiorly, the tumour abuts the left sublingual gland (asterisk). Medially, the lesion just crosses the midline, invading the superior portion of the lingual septum (arrow). The left genioglossus muscle (white arrowhead) and mylohyoid muscle (black arrowhead) are also shown for reference.
Floor of the mouth

Cancers arising in the anterior floor of the mouth spread readily within the sublingual space, crossing the midline anteriorly and invading the tongue, as well as extending anteriorly and laterally onto the mandible and gingiva. Less frequently, tumours extend posteriorly along the sublingual space to reach the submandibular space, penetrate through the mylohyoid muscle into the submental tissues, and may spread perineurally along the lingual nerves towards the skull base. Neoplasms arising from the sublingual glands are rare, and most are salivary malignancies.

Palatal tumours

Most hard palate tumours are salivary gland neoplasms, and over half of these are benign, notably pleomorphic adenomas. SCCs account for just over half of malignant palatal tumours, followed by minor salivary malignancies (30). Palatal SCCs frequently extend onto the upper alveolus and soft palate. Bony invasion of the hard palate and alveolus can also occur, with subsequent extension into the nasal cavity and maxillary sinus, respectively. Tumours reaching the posterior hard palate can spread via the greater and lesser palatine canals to the pterygopalatine fossa and skull base. The course of these nerves from the palate to the skull base should be examined meticulously, especially as perineural spread can be discontinuous (Figure 1.8).

Lymphatic spread of oropharyngeal cancers is initially to lymph nodes at level I (submandibular and submental groups) and level II (high jugular group). Bilateral nodal metastases are common, especially for tumours of the floor of the mouth and palate, and other groups including retropharyngeal and parotid nodes may also be involved.

Differential diagnosis

The differential diagnosis for early SCCs includes various benign and premalignant mucosal and submucosal lesions, including leukoplakia (white lesions), erythroplakia (red lesions), papillomas, hyperplasia, and necrotizing sialometaplasia. These may be indistinguishable from superficial cancers clinically and require biopsy for definitive diagnosis. Benign salivary conditions such as sublingual sialadenitis and floor of mouth retention cysts (ranulas) may produce intraoral masses but can be diagnosed readily on imaging. Odontogenic cysts and tumours usually have different clinico-radiological features to SCCs but may be difficult to differentiate, especially if there is overlying mucosal ulceration. Non-odontogenic tumours in the maxillofacial skeleton may rarely mimic invasive SCCs including osteosarcoma (typically affecting younger patients), mandibular metastasis (patients may have a known malignancy), multiple myeloma (frequently associated with other bone lesions), and non-Hodgkin lymphoma (associated with nodal and/or extranodal localizations and usually no other risk factors for HNSCC).

Treatment

The treatment of oral cavity cancer is influenced by tumour location and extent. Small lesions can often be cured by wide local resection and subsequent surgical reconstruction, or by brachytherapy. Larger lesions are treated by radiotherapy, concomitant chemoradiotherapy, or a combination with surgery.

For tumours invading the mandible, mandibular resections vary depending on the degree of bony invasion, which may be partial (rim resection) or full thickness (segmental or total mandibulectomy). The vast majority of tongue resections are wide local excisions or partial glossectomies, which preserve at least one lingual neurovascular bundle to innervate the remaining tongue. For advanced tumours, chemoradiotherapy is generally preferred over a total glossectomy because complete absence of the tongue has a poor functional outcome including unsafe swallowing.

Figure 1.8  Patient presenting with right-sided unilateral facial headache and anaesthesia of the palate. Clinically, there was no evidence for a tumoural lesion. Axial plain T1W spin-echo MRI (a) shows a soft tissue mass lesion in the right pterygopalatine fossa (asterisk), extending anterolaterally along the wall of the maxillary sinus (double arrowhead), laterally in the infratemporal fossa (arrow), and posteriorly in the pterygoid canal (single arrowhead). Section somewhat lower (b) shows soft tissue thickening in the region of the greater palatine canal (containing the greater palatine nerve, large arrow) and along the posterolateral wall of the maxillary sinus (arrowheads); there is signal loss in the right bony pterygoid process (small arrows). At the level of the maxillary alveolar process (c), soft tissue thickening is seen at its palatal side (arrow) and vestibular side (arrowheads); the bone itself also shows signal loss (asterisk). These findings are highly suggestive of a malignant neoplasm, arising at the level of the palate, with extensive perineural tumoural spread. Deep biopsy revealed adenoid cystic carcinoma.
**Key points: Oral cavity tumours**

- Different oral cavity subsites pose different challenges to imaging, including neurovascular involvement, bone invasion, and perineural spread.
- Cross-sectional imaging is required for most oral cavity tumours.
- Tumour thickness on imaging can differ markedly from depth of invasion on pathology if tumours are ulcerated or exophytic.

**OROPHARYNGEAL TUMOURS**

**Clinical presentation**

Squamous cell carcinoma is the commonest malignant tumour of the oropharynx (90%). Common symptoms including odynophagia, dysphagia, otalgia, or a neck mass due to metastatic lymphadenopathy (especially in HPV-positive tumours), while some advanced tumours may present with trismus and deep-seated pain. HPV-positive oropharyngeal SCCs typically have smaller primary tumours, while some advanced tumours may have larger primary tumours but more advanced nodal disease than HPV-negative cancers at presentation (16).

**Staging and radiological features**

The T staging is based on tumour size and invasion of specific structures, as well as HPV status (Table 1.2 and Figure 1.9); the latter is determined by assays from biopsies of primary tumour or metastatic nodes including polymerase chain reaction (PCR) and *in situ* hybridization (ISH) techniques. In routine practice, P16 tumour suppressor gene overexpression on immunohistochemistry is used as the initial surrogate test for HPV status, reflecting the fact that P16 overexpression correlates highly with HPV positivity in oropharyngeal tumours and is universally available, relatively inexpensive, and straightforward to interpret. To maximize the specificity for the HPV subtypes implicated in OPSCC, HPV subtyping using ISH is also routinely performed in P16-positive cases (31).

Most oropharyngeal cancers arise either from the tongue base or the tonsil. Submucosal spread is a hallmark, especially in the tongue base, which is usually silent and often invisible or underestimated clinically, but accurately depicted on CT and MRI. Invasion of the extrinsic tongue muscles, especially the genioglossus and hyoglossus muscles, should be specifically excluded as this signifies locally advanced disease (T4a) (Figure 1.10). Anterolateral spread into the floor of the mouth can occur, with subsequent invasion of the mandible. Posterior invasion across the glossotonsillar sulcus to the tonsil is also common. Vallecular tumours can spread directly onto the epiglottis, which is visible clinically, but can also penetrate through the floor into the pre-epiglottic space (part of the larynx), which is invisible clinically. Involvement of the pharyngeal (ventral) mucosal surface of the epiglottis is classified as T3 disease, whereas involvement of the laryngeal surface or pre-epiglottic space constitutes T4 disease. The extent of tongue base involvement influences treatment; superficial lateralized cancers that do not cross the midline are potentially resectable because only one lingual neurovascular bundle may need to be sacrificed.

Tonsillar cancers commonly arise along the anterior pillar but often involve other sites at diagnosis and may reach a substantial size within the fossa without spreading elsewhere, which may include T3 disease (>4 cm). Nevertheless, these cancers frequently spread locally to the tongue base, soft palate, retromolar trigone, and posterior oropharyngeal wall (Figure 1.11). Extrapharyngeal extension laterally can also occur, which is best appreciated on cross-sectional imaging as blurring of the normally visible overlying constrictor muscle, and from here, tumours can directly infiltrate the medial pterygoid muscle (Figure 1.12) as well as extend posterolaterally within the parapharyngeal space, where they may encroach on the carotid arteries (Figure 1.13). Superior extension, either mucosally to the nasopharynx or extramucosally within the parapharyngeal fat to the skull base, is uncommon.

Approximately 95% of tumours of the soft palate are SCCs. Although they may be small and lateralized, they frequently cross the midline as well as extend to the tonsil and hard palate. Less commonly, they extend along the mucosa superiorly to the nasopharynx or directly along the veli palatini muscles to the skull base (Figure 1.14) (32). Tumours at the junction of the soft and hard palate may extend perineurally within the palatine canals.

Tumours of the posterior oropharyngeal wall are rare and usually secondary to spread from other sites, especially the tonsil. They may be extensive at presentation due to clinically silent growth, which may be submucosal, reaching the oro- and hypopharynx. Tumour invasion posteriorly into the retropharynx and laterally into the

---

**Table 1.2 T staging of oropharyngeal carcinoma**

<table>
<thead>
<tr>
<th>Tis</th>
<th>Carcinoma in situ</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour &lt;2 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour &gt;2 cm but &lt;4 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour measures &gt;4 cm in greatest dimension or extends to mucosal surface of epiglottis*</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumour invades any of the following: larynx, deep/ extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), medial pterygoid muscle, hard palate, and mandible</td>
</tr>
<tr>
<td>T4b*</td>
<td>Tumour invades any of the following: lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, skull base, or encases the carotid artery</td>
</tr>
</tbody>
</table>

*For tumours of tongue base or vallecula specifically, extension to mucosal surface of the epiglottis constitutes T3 disease.
* T4b group is only applicable for p16/HPV negative cancers or if P16/HPV status is unknown. For P16/HPV positive cancers, T4a and T4b criteria are combined and designated as T4a.

**Source:** Adapted from Brierley JD et al. (2017).
parapharyngeal spaces are common. Deep invasion through the prevertebral fascia into the prevertebral muscles is uncommon and carries a poor prognosis. Demonstrating prevertebral muscle invasion on imaging is inaccurate. In this respect, the presence of an intact plane of fat in the retropharynx between the tumour and the prevertebral muscles on CT or MRI is highly predictive of the absence of prevertebral muscle invasion, but the loss of the fat plane or abnormal signal/attenuation or thickening or enhancement in the prevertebral muscles abutting the tumour can represent invasion or coexisting inflammation (33,34). To avoid erroneous overstaging, equivocal cases of prevertebral invasion that are otherwise resectable may be assessed by open exploration before proceeding to definitive resection.

Locally advanced disease depends on the primary site and is present if there is invasion of extrinsic tongue muscles, the nasopharynx, skull base, mandible, larynx, pterygoid muscles, prevertebral muscles, and carotid artery encasement (Figure 1.13). Invasion of the skull base or adjacent structures (e.g. lateral pterygoid muscle) is uncommon and associated with poor prognosis (Figure 1.14).

Lymphatic spread usually occurs in a sequential manner from superior to inferior, with the upper jugular chain lymph nodes (level II) being the first nodes at risk for lymphatic spread. Retropharyngeal nodal involvement may also occur (Figures 1.11 and 1.12), especially from tonsillar and palatal tumours. Bilateral nodal metastases are more common in midline cancers, especially the base of the
Tumours of the oral cavity and pharynx

Extranodal extension (ENE) is an important independent prognostic indicator in HNSCC, discussed in the section ‘Neck lymph node staging’.

Differential diagnosis

Enlargement of the lymphoid tissue in the tongue base, tonsillar fossa, and nasopharynx is commonly encountered and is mainly due to benign lymphoid hyperplasia; this is usually more avidly enhancing than squamous cell carcinoma or nasopharyngeal carcinomas, although there can be overlap. As mentioned previously, mild physiological asymmetry of the palatine tonsils is not uncommon, nevertheless any asymmetry should be documented and correlated clinically; depending on the clinical context, diagnostic biopsies may be required to exclude cancer. Oropharyngeal infections (e.g. acute tonsillitis and paratonsillar abscess) are usually distinguishable from malignancy clinically and radiologically, although uncommon chronic infections and granulomatous diseases may overlap.

Lymphoid tissue within the oral cavity and pharynx can be involved in non-Hodgkin lymphoma primarily or as part of systemic lymphoma. Most are of B-cell lineage and typically appear as bulky, homogeneous masses involving one or more sites in Waldeyer’s ring, which can be symmetrical or asymmetrical. These masses tend to displace rather than infiltrate adjacent tissues for their size and characteristically have markedly restricted diffusion on DWI. Cervical lymphadenopathy may be also present, with involved nodes typically being well circumscribed, rounded, and homogeneous, although nodal necrosis, margin irregularity, and extranodal invasion can occur, especially in the diffuse large B-cell subtype (35).

Minor salivary gland tumours are uncommon in the oropharynx and are usually mucoepidermoid and adenoid cystic carcinomas, although pleomorphic adenomas are more common in the soft palate. Primary tumours may be well circumscribed, containing areas with markedly high T2 signal and cystic foci; these features should suggest a salivary neoplasm as they are uncommon in primary tumours from SCC (Figure 1.15).

Treatment

Oropharyngeal SCC is treated definitively with either radiotherapy or surgery for early disease, and radiotherapy, chemoradiotherapy with or without surgery for advanced

Figure 1.10 Axial T2W MRI showing a bulky left base of tongue squamous cell carcinoma (black asterisk). There is displacement and frank invasion of the left geniohyoid/genioglossus muscle (white broken arrow) and hyoglossus muscle (white arrow), which indicate T4 disease. The left lingual artery is also encased (black arrow), and there is also posterolateral invasion beyond the pharynx into the left parapharynx (black broken arrow). The left sublingual gland is conspicuous on this axial section (white asterisk) due to displacement of tissues rather than invasion. The left mylohyoid muscle is also indicated for reference (white arrowhead).

Figure 1.11 Axial CECT images of a right-sided oropharyngeal cancer. (a) A soft tissue mass is visible in the tongue base (arrows). (b) At a slightly higher level, the lesion (arrows) extends across the glossoptonsillar sulcus (black arrow) into the anterior tonsillar pillar, and there is slight soft tissue thickening and increased enhancement on the soft palate (arrowhead). (c) There is a right necrotic metastatic retropharyngeal and a prominent indeterminate left retropharyngeal node (arrows).
disease. Radiotherapy is generally preferred over surgery for organ preservation including speech, swallowing, and airway protection, especially for palatal or tongue base cancers, although long-term side effects of radiation can be functionally debilitating. In recent years, minimally invasive surgical techniques including transoral laser microsurgery (TLM) and, more recently, transoral robotic surgery (TORS) have improved surgical options for patients with appropriately selected oropharyngeal cancers. Preliminary evidence suggests that survival and outcomes in OPSCC after TORS are comparable to definitive radiotherapy, while avoiding the chronic complications of radiotherapy (36).

For patients with HPV-associated OPSCC, clinical trials of de-intensified therapeutic regimens are presently under investigation to lower treatment-related toxicities (37).

**Figure 1.12** (a) Axial T2W and (b) plain T1W spin-echo MRI in a patient with an oropharyngeal cancer on the left side. The soft tissue mass involves the palatine tonsil, invades through the pharyngeal constrictor muscle into the parapharyngeal space (thick arrows), reaches the retromolar trigone (thin arrow), and compresses slightly the tongue base (thin arrowheads). A metastatic left retropharyngeal node is present (white asterisk). Normal pharyngeal constrictor muscle on right side (thick arrowheads); normal right parapharyngeal space (black asterisk).

**Figure 1.13** Axial CECT showing a locally advanced left oropharyngeal cancer arising from the left lateral wall. Within the pharynx, tumour extends medially across the left side of the soft palate (black arrowhead) and anterolaterally to the retromolar trigone (black asterisk). There is gross lateral invasion through the pharynx and beyond the parapharyngeal space, with invasion of the left medial pterygoid muscle in the masticator space (black arrow) and the left parotid deep lobe (white arrowhead). Tumour abuts the left internal carotid artery by 150° (white arrow). Note the normal fat in the right parapharyngeal space (white asterisk).

**Figure 1.14** Coronal T1W post-contrast MRI showing a locally advanced left oropharyngeal SCC arising from the left soft palate and tonsil. There is gross lateral invasion of the left parapharyngeal fat and the medial and lateral pterygoid muscles and extension along the left veli palatini muscles to just beneath the left skull base. The uvula is also invaded and deviated towards the tumour (white asterisk). Normal right-sided structures are as follows: medial pterygoid muscle (black arrow), lateral pterygoid muscle (white arrow), tonsil (white arrowhead), veli palatini muscles (white arrowhead), and parapharyngeal fat (black asterisk).
Tumours of the oral cavity and pharynx

NASOPHARYNGEAL TUMOURS

Clinical presentation

The most common nasopharyngeal malignancy, nasopharyngeal carcinoma (NPC), is classified by the World Health Organization (WHO) into three types: keratinizing squamous cell carcinoma (type I), non-keratinizing squamous cell carcinoma (type II), and undifferentiated carcinoma (type III). Type III is the most common and is endemic in regions of the world such as China, Southeast Asia, and North Africa. NPC is more common in males, arises at any age but is predominantly a disease of middle age, and is linked to the Epstein–Barr virus (EBV) and genetic and dietary factors. There is a four-fold increase in subjects with a first-degree family history of NPC (38). Common presenting symptoms include epistaxis, nasal blockage, and hearing loss secondary to dysfunction of the eustachian tube. However, early-stage disease can be clinically silent, and commonly NPC presents only in the more advanced stages when it has invaded deep structures, such as the brain and cranial nerves, or spread to lymph nodes in the neck.

Detection

MRI has a pivotal role in the detection of NPC because it can detect the 10% of NPCs that are endoscopically occult (39). These are usually small tumours hidden from view in the pharyngeal recess mucosa (Rosenmüller’s fossa) or in the submucosa. MRI is used to detect NPC in symptomatic patients who have a normal endoscopic examination but high clinical suspicion of NPC. MRI can also detect early-stage NPC in asymptomatic subjects from family and population screening programs who have a positive plasma EBV-DNA blood test and a normal endoscopic examination (40).

Staging and radiological features

Imaging is required for both staging and treatment planning. MRI depicts patterns of primary tumour and nodal spread down the neck (41,42) and is the preferred modality for mapping the primary tumour boundary and its relationship to complex adjacent structures in the parapharynx, retropharynx, skull base, and brain, as well as discrimination from adjacent retropharyngeal nodes (43). Both CT and MRI are used by radiotherapists for radiotherapy planning. Ultrasound with or without fine needle aspiration is used for those occasional indeterminate nodes that have a major influence on management. The main advantage of FDG PET-CT is the detection of distant metastases, but the incidence is low at diagnosis so it tends to be reserved for patients at high risk of distant metastases. A structured head and neck radiology report organized according to the T and N staging classification can be used to convey the radiology information in a clear, concise, and predictable manner, allowing the radiotherapist and oncologist to extract the pertinent information.

Primary tumour staging

T staging is summarized in Table 1.3 and Figure 1.16. Size is not a criterion for NPC T staging in T1, the tumour is confined to the nasopharynx or extends to the oropharynx

Key points: Tumours of the oropharynx

- Most oropharyngeal SCCs arise from the anterior tonsillar pillar and tongue base.
- Submucosal tumour extension within the oropharynx is common.
- In tumours of the tongue base, extension across the midline usually precludes surgical cure.
- Early tonsillar and tongue base primary SCCs can be radio logically occult.
- PET-CT may disclose small tongue base or tonsillar cancers that are equivocal or hidden on CT and MRI.
- The tonsillar fossa is a prime site for lymphoma.

Table 1.3  T staging of nasopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour confined to nasopharynx, or extends to oropharynx and/or nasal cavity without parapharyngeal involvement</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour with extension to parapharyngeal space and/or infiltration of the medial pterygoid, lateral pterygoid, and/or prevertebral muscles</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour invades bony structures of skull base, cervical vertebra, pterygoid structures, and/or paranasal sinuses</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, parotid gland and/or infiltration beyond the lateral surface of the lateral pterygoid muscle</td>
</tr>
</tbody>
</table>

Source: Adapted from Brierley JD et al. (2017).
Nasopharyngeal staging.

**Stage T1**

*Nasopharynx*

The nasopharynx lies behind the nasal cavity and above the oropharynx, the soft palate forming the inferior wall. NPC is confined to the nasopharynx when it involves the roof (containing the centrally placed adenoid), posterior wall, and lateral walls, including the pharyngeal recesses, eustachian tube entrance, torus tubarius, and levator palatini muscle attached to the tube (Figure 1.17a).
Tumours of the oral cavity and pharynx

The pharyngeal recess is a common site for NPC (Figure 1.17a), and small tumours deep in the recess can be identified easily on MRI but may be undetectable on nasoendoscopy because of angulation of the recess and the fact that the walls of the recess are often collapsed.

Nasal cavity and oropharynx

Superficial tumour spread to the nasal cavity is common, but it is less common in the oropharynx. NPC has a predilection for superior, rather than inferior, spread, and thus, oropharyngeal tumour beyond the soft palate should initiate a search for tumour spread elsewhere.

Stage T2

Parapharynx and retropharynx

Tumour spreads into the lateral/posterolateral parapharynx by directly invading through the levator palatini muscle and pharyngobasilar fascia, or by passing through a gap where the eustachian tube penetrates the fascia. The pharyngobasilar fascia forms a thin black line on the T2 and T1 post-contrast images, which can be identified along the lateral and postero-lateral aspect of the nasopharynx. The fascia is best seen when directly abutted by tumour and invasion causes a disruption of this line. Parapharyngeal structures invaded by tumour are the tensor palatini muscle, fat-filled parapharyngeal space, and medial and lateral pterygoid muscles, as well as the carotid sheath (Figure 1.17b). Tumour spreads also directly posteriorly into the retropharynx (Figure 1.17b) to invade the preclival/prevertebral muscles, prevertebral fat and fascia, Batson’s venous plexus, and a web of lymphatic channels. Tumour may spread preferentially down the retropharynx to the cervical level.

Stage T3

Skull base

NPC has a predilection for skull base invasion (Figure 1.18), invading the cortex before spreading, often extensively, through the bone marrow. MRI is sensitive to bony invasion (44), which is identified when the bony abnormality is in continuity with the primary tumour and is of similar signal intensity on all sequences. NPC also causes sclerosis, seen as low signal intensity (Figure 1.18).

Figure 1.17  Axial T1W post-contrast MRI showing (a) small stage T1 NPC confined to the mucosa of the pharyngeal recess (short arrow) and posterior wall on the right side. Normal levator palatini muscle (1), tensor palatini muscle (2), eustachian tube orifice (3), torus tubarius (4), medial pterygoid muscle (5), lateral pterygoid muscle (6), and parapharyngeal fat space (7); (b) stage T2 NPC of the parapharynx (short arrows) invading through the levator palatini muscle, into the tensor palatini muscle, parapharyngeal fat space, and medial pterygoid muscle. The tumour also abuts the internal carotid artery (open arrow) and invades the retropharynx (long arrow).

and b). The pharyngeal recess is a common site for NPC (Figure 1.17a), and small tumours deep in the recess can be identified easily on MRI but may be undetectable on nasoendoscopy because of angulation of the recess and the fact that the walls of the recess are often collapsed.

Nasal cavity and oropharynx

Superficial tumour spread to the nasal cavity is common, but it is less common in the oropharynx. NPC has a predilection for superior, rather than inferior, spread, and

Figure 1.18  Sagittal T1W MRI showing a stage T3 NPC in the nasopharynx (short arrows) invading the skull base (open arrows) and the sphenoid sinus (long arrow). There is diffuse sclerosis of the clivus.
Important sites to check are summarized as follows:

1. **Five major bony sites** comprising (1) right pterygoid, (2) left pterygoid, (3) clivus, (4) right petrous apex, and (5) left petrous apex (Figure 1.19a and b), which can all be assessed initially on the axial T1WI image just above the nasopharynx. Additional sagittal and coronal planes are needed to assess the superior clivus and the sphenoid bone surrounding the sphenoid sinus (which includes the sphenoid sinus floor/nasopharyngeal roof). Mild invasion of any of these bones bordering the nasopharynx may be the only site of tumour invasion outside the nasopharynx, including the medial borders of the pterygoid bones which are not protected by a layer of fascia. More extensive invasion may involve the sphenoid wings, foramen magnum, and occipital condyles.
2. **Three major foramina** from anterior to posterior on the coronal images (Figure 1.20a to c) comprising (1) foramen rotundum (containing the V2 nerve), (2) foramen ovale (containing the V3 nerve), and (3) foramen lacerum which is directly below the horizontal portion of the internal carotid artery. The other foramina are the sphenopalatine foramen, jugular foramen, and foramen spinosum.

3. **Three major canals** from superior to inferior on axial images (Figure 1.21a to c) comprising (1) vidian canal (contains the vidian nerve), which runs horizontally from the pterygopalatine fossa to the foramen lacerum, providing a route for tumour spread between the anterior and posterior skull base (also well seen on coronal images [Figure 1.20b]); (2) pterygopalatine canal (contains the greater and lesser palatine nerves), which runs vertically down to the palate; and (3) hypoglossal canal (contains the XII nerve and a venous plexus which should not be mistaken for enhancing tumour). The other canals are the infraorbital canal, involved by V2 perineural spread, and the optic canal.

4. **Three major fissures** comprising (1) pterygomaxillary fissure, along the posterior wall of the maxillary sinus (Figure 1.21a); (2) orbital (inferior [Figure 1.22] and superior) fissures; and (3) petroclival fissure extending between the clivus and petrous apex.

5. **Pterygopalatine fossa** which is a pyramidal fat-filled space containing the V2 nerve and pterygopalatine ganglion, most easily located at the medial end of the pterygomaxillary fissure on the axial images (Figure 1.21a). The pterygopalatine fossa is a danger zone because tumour from this site can spread to the medial wall of the nasal cavity (via the sphenopalatine foramen), infratemporal fossa (via the pterygomaxillary fissure), orbit (via the inferior orbital fissure), brain (via the foramen rotundum), internal carotid artery (via the vidian canal), and palate (via the pterygopalatine canal) (Figures 1.21a and 1.22).

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**Figure 1.21** Axial T1W post-contrast MRI showing the three-main skull base canals invaded by NPC (open arrows). From superior to inferior (a) left vidian canal showing tumour spreading between the pterygopalatine fossa (*) and foramen lacerum (short white arrows). Tumour also extends along the left pterygomaxillary fissure (long arrow) to the infratemporal fossa; (b) left pterygopalatine canal which extends vertically from the pterygopalatine fossa above to the palate below; (c) both hypoglossal canals which are invaded from tumour in the retropharynx. Tumour spread is seen in the infratemporal fossa (long arrows) anterolateral to the lateral pterygoid muscles, which are invaded also by the tumour.

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**Cervical spine**

The cervical spine, especially the anterior arch of C1, is invaded by tumour extending down the retropharyngeal soft tissues or the clivus.

**Paranasal sinuses**

The sphenoid sinus lies immediately above the nasopharynx, being separated only by a thin bony shelf, so it is usually the first sinus to be invaded by NPC, followed by the ethmoid sinuses and maxillary sinuses (usually seen only in very advanced stage disease).

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**Figure 1.22** Coronal T1W post-contrast MRI showing NPC in the left pterygopalatine fossa (*) with medial spread through the sphenopalatine foramen to the nasal cavity (open arrow), inferior spread along the pterygopalatine canal to the palate (long arrow), and superior spread along the inferior orbital fissure to the orbit (short arrow).
Stage T4

Brain and cranial nerves

The cavernous sinus (Figure 1.20b and c) and dura of the middle and posterior cranial fossa are the most common intracranial sites for tumour invasion; direct invasion of the temporal lobe is rare. The cavernous sinus is invaded via bone, foramina, cranial nerves, or along the internal carotid artery. V2, V3, VI, and XII are the cranial nerves most commonly involved by direct tumour encasement in the skull base or brain, but perineural spread may occur notably along the V2 nerve in the infraorbital canal towards the cheek and the V3 nerve below the skull base in the parapharyngeal fat space (Figure 1.20b) (to distant branches including the auriculotemporal nerve which communicates with the VII nerve in the parotid gland). Muscle denervation leads to oedema, enhancement, and, later, atrophy and can be found in the muscles of mastication (Figure 1.20b) supplied by V3 and muscles of the hemitongue supplied by XII.

Infratemporal fossa

The infratemporal fossa is the area that lies anterolateral to the lateral pterygoid muscle containing fat and muscle (Figure 1.21c). It is usually invaded via the pterygomaxillary fissure or through the lateral pterygoid muscle.

Orbit, parotid gland, and hypopharynx

The orbit is invaded via the orbital fissures/optic canal from tumour in the cavernous sinus or pterygopalatine fossa. The parotid gland is a recent addition to the staging classification. The hypopharynx is rarely invaded by tumour.

Nodal metastases

NPC has a propensity to spread to cervical nodes. The diagnostic criteria for identifying metastatic nodes are the same as those for other carcinomas of the head and neck, but nodal staging (N staging) is different (details of nodal staging and nodal levels are shown in the section ‘Neck lymph node staging’). NPC nodal metastases may occur in the presence of small primary tumours, are frequently bilateral, bulky, and necrotic, and show extranodal extension. Lateral retropharyngeal or upper internal jugular chain nodes (level II), especially those that lie posterior to the internal jugular vein (level IIA or B), are the first echelons of nodal spread (42,45). Medial retropharyngeal nodes rarely form discrete nodes, but diffuse plaques of enhancement may be seen along the retropharyngeal lymphatic plexus. Metastatic nodes follow an orderly spread down the internal jugular chain (levels III and IV) or spinal accessory chain in the posterior triangle (levels VA and VB) to the lower neck and then to the mediastinum or axilla. Skip metastases are rare. Parotid (intra- and periparotid), submental (level Ia), and submandibular (level IB) nodal metastases are uncommon and tend to be associated with ipsilateral nodal disease in level II. Advanced nodal stage (N3) is the strongest imaging predictor for distant metastases (46) (Figure 1.23).

Differential diagnosis

Less-common malignancies of the nasopharynx include lymphoma, adenoid cystic carcinoma, and sarcoma. Radiological differentiation may not be possible, although there are features that should raise suspicion of these other tumours. Imaging features that favour non-Hodgkin lymphoma of the nasopharyngeal adenoid are an exophytic tumour that is large without deep tumour invasion, multifocal disease, and abnormal lymph nodes (non-necrotic or necrotic), which are located outside the routes of usual NPC nodal spread (parotid, submandibular, submental, and external jugular chain). Adenoid cystic carcinoma should be considered when perineural spread distant to the main bulk of the tumour is a prominent feature of the disease, and rhabdomyosarcoma should be considered in children presenting with a large tumour invading neighbouring structures.

Treatment

Treatment of NPC is by radiotherapy with or without chemotherapy and may also include new targeted systemic therapies (47). NPC is responsive to radiotherapy, which is nowadays delivered as intensity-modulated radiotherapy using a high dose of 70 Gy to the primary tumour and...
nodal metastases. Lower doses are delivered to surrounding normal tissues, normal nodes, and tumour sites adjacent to sensitive structures such as the brain stem, cervical spine, and brachial plexus. The parotid and submandibular glands are spared to reduce xerostomia unless there are metastatic nodes in or adjacent to these glands. The extent of the primary tumour and nodal metastases on imaging is used to plan the radiotherapy field. Early-stage disease is treated by radiotherapy alone, while advanced locoregional disease (T3/T4 and/or N2/N3) is treated by concurrent chemoradiotherapy. Bulky primary or nodal tumours close to important structures may also undergo a course of neoadjuvant chemotherapy to shrink the tumour before the start of concurrent chemoradiotherapy. Indications for neoadjuvant chemotherapy include intracranial extension into the cavernous sinus and dura, extensive perineural spread, bulky retropharyngeal primary and nodal tumours, bulky oropharyngeal tumour (to reduce the severity of radiotherapy-induced mucositis), and nodes close to the brachial plexus. Chemotherapy is the main treatment for distant metastases, and surgery is reserved for operable locoregional tumour relapse.

**Key points: Tumours of the nasopharynx**

- MRI has a role in the detection of early-stage NPCs that are hidden from endoscopic view.
- A structured head and neck radiology report organized according to the T and N staging classification conveys the radiology information in a clear, concise, and predictable manner.
- Nasopharyngeal carcinoma has a high propensity for deep spread into sites that include the para/retropharynx, skull base, and brain. MRI is the preferred modality for mapping the extent of primary tumour spread for radiotherapy planning.
- Nasopharyngeal carcinoma has a high propensity for nodal spread. Nodal metastases spread in an orderly fashion down the neck, with the retropharyngeal and upper internal jugular nodes, especially those posterior to the internal jugular vein, being the first echelons of nodal spread. Metastatic nodes influence radiotherapy planning, especially those close to the salivary glands and brachial plexus.
- T3/T4 and N2/N3 disease are indications for concurrent chemoradiotherapy.

**HYPOPHARYNGEAL CANCER**

**Clinical presentation**

Hypopharyngeal tumours account for a small proportion of head and neck SCCs (3%–5%) (48). Although they can produce odynophagia, otalgia, and dysphagia, many primaries are silent or symptoms may be misattributed to gastroesophageal reflux such that disease is often advanced at presentation. Patients may also present with hoarseness due to laryngeal and/or recurrent laryngeal nerve involvement. One quarter of patients present with a neck mass due to metastatic nodal involvement (49).

**Staging and radiological features**

Most hypopharyngeal tumours arise in the piriform sinuses (65%–85%), followed by the posterior pharyngeal wall (10%–20%), and the postcricoid region (5%–15%), although multiple subsites are usually involved at diagnosis (60%) (49). Shallow tumours may not be visible on flexible endoscopy, and submucosal extension is especially common (60%), which can extend over 1 cm beyond clinically visible margins (50). The T stage is determined by tumour size, extent, and the presence of hemilaryngeal fixation, namely a fixed or poorly mobile cord. Hemilaryngeal fixation may result from invasion of the cricoarytenoid joint, posterior cricothyroid muscle, or the recurrent laryngeal nerve and is a clinical diagnosis although it can be observed on imaging (Table 1.4 and Figure 1.24). Two-thirds of tumours are locally advanced at presentation (T3/T4) (48).

Early piriform sinus tumours appear as mild mucosal asymmetry, which can be subtle and easily overlooked (Figure 1.25). Although tumours may initially involve a single wall, at presentation, they often are bulky and involve all walls as well as extend onto the posterior hypopharyngeal wall and/or post cricoid region, indicating at least T2 disease. Tumours arising on the aryepiglottic fold readily penetrate through the fold to encroach the supraglottic airway, as well as extend inferiorly to the cricoarytenoid joint, as well as extend inferioirly to the cricoarytenoid joint and posterior aspect of the glottis, producing cord fixation (T3). Sclerosis of the arytenoid or cricoid cartilages adjacent to the tumour may be seen on CT and MRI; this is non-specific and does not automatically signify cartilage invasion as it can be reactive. Tumours reaching the

**Table 1.4** T staging of hypopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>Tumour (size in greatest dimension)</th>
<th>Additional note</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Limited to 1 subsite of hypopharynx and/or &lt;2 cm</td>
<td>Subsites are the piriform sinuses, postcricoid, and posterior hypopharyngeal wall</td>
</tr>
<tr>
<td>T2</td>
<td>Invades ≥1 subsite or an adjacent site or measures ≥2 cm but ≤4 cm without fixation of hemilarynx</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>&gt;4 cm or with fixation of hemilarynx</td>
<td></td>
</tr>
<tr>
<td>T4a</td>
<td>Invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, central compartment soft tissue</td>
<td></td>
</tr>
<tr>
<td>T4b</td>
<td>Invades prevertebral fascia, encases carotid artery, or invades mediastinal structures</td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Adapted from Brierley JD et al. (2017).
Hypopharyngeal cancer

piriform sinus apex (level with the cricoarytenoid joint) frequently extend anteriorly through the cricothyroid gap into the posterior paraglottic fat, where they may spread extensively submucosally within the larynx, including reaching the pre-epiglottic fat; this submucosal spread may be invisible on endoscopy. Tumours may also invade directly through the thyrohyoid membrane, the thyroid cartilage, and the inferior constrictor muscle inserts onto the lateral surface of each thyroid cartilage approximately 1 cm in front of the posterior margin. Consequently, bulky piriform sinus cancers may wrap slightly around the posterior border of the ipsilateral thyroid cartilage while remaining deep to the constrictor muscle, and this appearance should not be mistaken for extrapharyngeal extension (Figure 1.26). Superiorly, tumours can extend along the lateral oropharyngeal wall onto the palatine tonsil.

Figure 1.24  Hypopharyngeal T staging diagram.
Tumours of the oral cavity and pharynx

Posterior hypopharyngeal wall cancers are frequently exophytic, bulky (>80% >5 cm), and extensive in terms of involving the oropharynx and/or cervical oesophagus at presentation (49). Direct invasion through the constrictor muscle into the retropharynx is also common (Figure 1.27), whereas deeper invasion into the prevertebral muscles is uncommon.

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A Figure 1.25  CECT images. (a) Axial image during quiet breathing shows subtle soft tissue thickening in the apex of the right piriform sinus (arrow; compare to opposite side). There is subtle infiltration or displacement of the paraglottic space fat (arrowhead). The right piriform sinus expands somewhat less than the opposite side; the soft tissue irregularity produced by the cancer is now more visible (arrowheads). Squamous cell carcinoma was diagnosed.

Figure 1.26  CECT image. Squamous cell cancer originating from the right piriform sinus, growing anteriorly in the paraglottic space, anterolaterally through the thyroid cartilage, and laterally through the lateral pharyngeal wall. The primary tumour is in direct contact with a metastatic right mid jugular lymph node (asterisk).

Differential diagnosis

Nearly all hypopharyngeal malignancies are SCCs. Rarely, sarcomas, minor salivary gland neoplasms, or plasmocytomas may occur here, which show non-specific imaging findings and are initially worked up in a similar way to SCC.

Treatment

Low-volume T1/T2 hypopharyngeal cancer can be effectively treated by radiation therapy alone (66–70 Gy) (48), although surgery can be performed with or without postoperative radiotherapy, depending on pathology findings. CT or MRI is helpful in selecting patients into a favourable group for radiation treatment by providing an estimate of tumour volume (51). More advanced hypopharyngeal tumours (T3/T4), if resectable, may be treated by partial pharyngectomy or total laryngopharyngectomy depending on the extent of disease; if the tumour extends to the oesophagus, an oesophagectomy is also required. Alternatively, organ preservation by using radiotherapy with altered fractionation or concurrent chemoradiotherapy are feasible alternatives (48). The imaging findings are essential in the multidisciplinary management of these patients.
Neck lymph node staging

Lymph node involvement is the single most important prognostic indicator in head and neck cancer, for example, halving the 5-year survival in HNSCC (52). Prognosis is further influenced by size and number of nodal metastases, bilateral or contralateral involvement, and extranodal extension (ENE) (53,54). Clinical evaluation of neck lymph nodes is imprecise, with false-negative and false-positive rates of 15%–25% and 30%–50%, respectively.

The radiological criteria used to diagnose neck lymphadenopathy on CT and MR studies are size and internal structure. The size criterion is a compromise between sensitivity and specificity. In practice, a minimum axial diameter of $\geq 10$ mm ($\geq 5$ mm retropharyngeal and $\geq 11$ mm jugulodiastric, or a group of 3 or more nodes $\geq 8$ mm), necrosis, or extracapsular spread are generally accepted criteria of abnormality. Using these criteria, the sensitivity of CT is about 90%, and the specificity is about 73%. The accuracies of CT and MRI are comparable. Metastatic nodes from SCC frequently contain areas of necrosis and frankly cystic areas which can be substantial such that a single cystic node in the lateral neck can resemble a branchial cleft cyst on imaging (55). As such, a lateral cystic neck mass in an adult should be regarded as a metastatic node until proved otherwise. Cystic nodes are also more common in HPV-positive compared with HPV-negative oropharyngeal SCCs (56).

The impact of imaging on patient management is high when lymphadenopathy, previously undetected clinically or at places beyond the planned treatment field, is seen. SCC, CT, or MRI shows lymphadenopathy in 7.5%–19% of clinically ‘N0 necks’ on palpation. Imaging may also detect lymphadenopathy in sites not accessible by clinical examination (e.g. retropharynx and paratracheal space).

None of the currently available anatomical imaging methods can reliably depict small tumour deposits in non-enlarged lymph nodes or differentiate reactively enlarged lymph nodes from metastatic lymphadenopathy. This can be partly overcome by combining ultrasonography with fine-needle aspiration cytology (US-FNAC). In N0 necks, a sensitivity of 73% and a specificity of 100% have been reported with this technique, significantly better than can be obtained with CT or MRI (Figure 1.28) (57). However, not all nodal groups are accessible by neck ultrasound, and the accuracy of US is highly operator dependent.

Detection of nodal metastases on MRI may be improved by the inclusion of DWI-MRI; malignant nodes typically show restricted diffusion compared with normal nodes, mainly due their high cellularity, whereas inflammatory lymph nodes show increased diffusion (58) (Figure 1.29). PET-CT may also suggest metastatic involvement in normal or equivocal nodes on conventional imaging by virtue of higher FDG uptake than would be expected for their size (Figure 1.27). Nevertheless, markedly necrotic or small/microscopic nodal metastases can produce false negatives on the PET component, and infective lymphadenopathies can produce false positives.
ENE of the tumour through the lymph node capsule is, with the exception for HPV-positive oropharyngeal SCC, a poor prognostic indicator in HNSCC, effectively halving the 5-year disease-free survival from 63% to 30% \((28,59)\). Only macroscopic ENE can be detected radiologically. Radiological irregular nodal contour and/or infiltration of adjacent planes (Figure 1.30) \((60,61)\). The sensitivity and specificity of US, CT, and MRI range between 77%–87% and 75%–85%, respectively \((62)\); false negatives may reflect minor/microscopic ENE, whereas false positives usually reflect concomitant inflammatory changes. The current eighth edition of the TNM classification includes ENE in N staging, although this is separated into clinical and pathological ENE. Pathological ENE is based on histology and may be minor or major, whereas clinical ENE must be unambiguous to avoid stage migration \((28)\). Accordingly, clinical ENE must be evident on physical examination (e.g. invasion of skin, infiltration of musculature/dense tethering to adjacent structures, or dysfunction of a cranial nerve, the brachial plexus, the sympathetic trunk, or the phrenic nerve), which may be supported by radiological findings.

Invasion of the common or internal carotid arteries by tumour in HNSCC usually indicates unresectable disease and carries a poor prognosis \((63)\). The accuracy of imaging for carotid invasion is suboptimal although the likelihood of invasion is low if tumour contacts the vessel by under 90° of its circumference, and high but not invariably present if over 270° \((64)\) (Figure 1.13).

![Figure 1.28](image)

**Figure 1.28** Grey scale with power Doppler US of two lymph nodes in different patients. (a) Normal lymph node in right level IIA (jugulodigastric) with normal shape, smooth margin, uniform cortical echogenicity, an echogenic hilum (white arrow) and a hilar pattern of vascularity. A normal adjacent submandibular gland is also shown (white asterisk). (b) A pathological lymph node in right level III (mid-jugular) which was clinically impalpable (clinical N0). Despite its normal size (6 mm short axis diameter) and shape, this node is heterogeneous with subtle hypoechoic regions suggestive of necrosis or tumour infiltration (black arrows). The normally echogenic hilum is also absent and the node displays abnormal pericapsular vessels (white arrowhead) rather than a hilar pattern vascularity. US-guided FNAC of a hypoechoic region revealed a metastatic lymph node from SCC. This metastatic node was not detected on CT (not shown).

![Figure 1.29](image)

**Figure 1.29** Gadolinium-enhanced, T1W turbo spin-echo (TSE) MRI (a) shows a large tumour (arrows) in the left side of the oral tongue. An ipsilateral level II (b, arrow), node has a normal-shape, regular contour, short axis diameter of 0.8 cm, and shows homogeneous contrast-enhancement. This may be regarded as a normal node on anatomic MRI sequences. Nevertheless, this node is hyperintense on (c) b 0 and (d) b 1000 diffusion-weighted images (arrows), with (e) a low ADC of \(0.7 \times 10^{-6} \text{ mm}^2/\text{sec}\), thus is suspicious for metastatic involvement. Histopathology confirmed a large metastatic deposit in this lymph node.
Neck lymph node staging

The level system of lymph node classification is a nomenclature dividing cervical lymph nodes into seven regions or ‘levels’; some lymph nodes are not part of any of these levels and are described by their anatomical location (e.g. retropharyngeal nodes, parotid nodes, facial nodes) (Table 1.5, Figure 1.31) (65).

Nodal staging in head and neck cancer

Nodal staging differs between P16 negative SCCs of the head and neck (non-cutaneous) (Table 1.6), P16 oropharyngeal positive cancers (Table 1.7), and NPC (Table 1.8) (29); in all three, N0 indicates no regional nodal metastasis. A separate nodal classification for HPV-positive OPSCCs has been introduced recently, differing from non-HPV cancers.

Figure 1.30  Axial T1W (a) and T1W post-contrast with fat saturation (b) MRI of a large left upper jugular nodal metastasis with irregular ill-defined margins that is contiguous with the left sternocleidomastoid muscle (white arrow), left parotid gland (black arrowhead), and the left posterior parapharyngeal space (carotid space). This mass was fixed clinically, thus clinically and radiologically compatible with extranodal extension. The primary tumour was not identified including after exhaustive work-up including panendoscopy, cross-sectional imaging and PET-CT (not shown), and biopsy of at-risk sites. Biopsy of the metastatic node was negative for EBV and P16/HPV markers, thus staged as for an HPV-negative carcinoma with extranodal invasion (Tx N3 disease).

Table 1.5  Imaging-based neck nodal classification

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Submental and submandibular nodes</td>
</tr>
<tr>
<td>Level IA</td>
<td>Submental nodes, between the medial margins of the anterior bellies of the digastric muscles</td>
</tr>
<tr>
<td>Level IB</td>
<td>Submandibular nodes, lateral to level IA nodes and anterior to the back of the submandibular salivary gland</td>
</tr>
<tr>
<td>Level II</td>
<td>Upper internal jugular nodes, posterior to the back of the submandibular salivary gland, anterior to the back of the sternocleidomastoid muscle, and above the level of the bottom of the body of the hyoid bone</td>
</tr>
<tr>
<td>Level III</td>
<td>Middle jugular nodes, between the level of the bottom of the body of the hyoid bone and the level of the bottom of the cricoid arch, anterior to the back of the sternocleidomastoid muscle</td>
</tr>
<tr>
<td>Level IV</td>
<td>Low jugular nodes, between the level of the bottom of the cricoid arch and the level of the clavicle, anterior to a line connecting the back of the sternocleidomastoid muscle and the posterolateral margin of the anterior scalene muscles; they are lateral to the carotid arteries</td>
</tr>
<tr>
<td>Level V</td>
<td>Posterior triangle nodes, posterior to the back of the sternocleidomastoid muscle, and posterior to the line described in level IV</td>
</tr>
<tr>
<td>Level VA</td>
<td>Above the level of the bottom of the cricoid arch</td>
</tr>
<tr>
<td>Level VB</td>
<td>Between the level of the bottom of the cricoid arch and the level of the clavicle</td>
</tr>
<tr>
<td>Level VI</td>
<td>Upper visceral nodes, between the carotid arteries from the level of the bottom of the body of the hyoid bone to the level of the top of the manubrium</td>
</tr>
<tr>
<td>Level VII</td>
<td>Superior mediastinal nodes, between the carotid arteries below the level of the top of the manubrium and above the innominate vein</td>
</tr>
<tr>
<td>Supraclavicular nodes</td>
<td>Nodes at, or caudal to, the level of the clavicle and lateral to the carotid artery</td>
</tr>
<tr>
<td>Retropharyngeal nodes</td>
<td>Nodes behind the pharynx, medial to the internal carotid artery, from the skull base down to the level of the hyoid bone</td>
</tr>
</tbody>
</table>

Source: Adapted from Som et al. (1999).
Figure 1.31 Level system of lymph node classification. Diagram of the neck as seen from the left anterior view: (a) the pertinent anatomy that relates to the nodal classification and (b) an outline of the levels of the classification. Note that the line of separation between levels I and II is the posterior margin of the submandibular gland. The separation between levels II and III and level V is the posterior edge of the sternocleidomastoid muscle. However, the line of separation between levels IV and V is an oblique line extending from the posterior edge of the sternocleidomastoid muscle to the posterolateral edge of the anterior scalene muscle. The posterior edge of the internal jugular vein separates level IIA and IIB nodes. Level VI nodes are medial to the internal carotid arteries and below the hyoid bone and above the manubrium. The top of the manubrium separates levels VI and VII.
Table 1.6 Clinical N staging of oral and hypopharyngeal carcinoma and p16-negative oropharyngeal carcinoma

<table>
<thead>
<tr>
<th>Nodal stage</th>
<th>Number and site nodal metastases</th>
<th>Size (maximum dimension)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>Single ipsilateral node</td>
<td>≤3 cm, no ENE</td>
</tr>
<tr>
<td>N2a</td>
<td>Single ipsilateral node</td>
<td>&gt;3 cm but ≤6 cm, no ENE</td>
</tr>
<tr>
<td>N2b</td>
<td>Multiple ipsilateral lymph nodes</td>
<td>&lt;6 cm, no ENE</td>
</tr>
<tr>
<td>N2c</td>
<td>Bilateral or contralateral lymph nodes</td>
<td>&lt;6 cm, no ENE</td>
</tr>
<tr>
<td>N3a</td>
<td>Any</td>
<td>&gt;6 cm, no ENE</td>
</tr>
<tr>
<td>N3b</td>
<td>Single or multiple lymph nodes</td>
<td>Clinical ENE</td>
</tr>
</tbody>
</table>

Source: Adapted from Brierley JD et al. (2017).

Abbreviation: ENE Extra nodal extension.

Table 1.7 Clinical N staging of HPV/P16-positive oropharyngeal SCC

<table>
<thead>
<tr>
<th>Nodal stage</th>
<th>Number and site nodal metastases</th>
<th>Size (maximum dimension)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>≥1 ipsilateral nodes</td>
<td>≤3 cm</td>
</tr>
<tr>
<td>N2</td>
<td>Contralateral or bilateral nodes</td>
<td>≤6 cm</td>
</tr>
<tr>
<td>N3</td>
<td>Any</td>
<td>&gt;6 cm</td>
</tr>
</tbody>
</table>

Source: Adapted from Brierley JD et al. (2017).

Table 1.8 N staging of nasopharyngeal carcinoma

<table>
<thead>
<tr>
<th>Nodal stage</th>
<th>Number and site nodal metastases</th>
<th>Size (maximum dimension)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N1</td>
<td>Unilateral cervical nodes (any number) and/or unilateral or bilateral retropharyngeal nodes</td>
<td>≤6 cm above the caudal border of cricoid cartilage</td>
</tr>
<tr>
<td>N2</td>
<td>Bilateral cervical nodes (any number)</td>
<td>≤6 cm above the caudal border of cricoid cartilage</td>
</tr>
<tr>
<td>N3</td>
<td>Cervical node(s)</td>
<td>&gt;6 cm and/or extension below caudal border of cricoid cartilage</td>
</tr>
</tbody>
</table>

Source: Adapted from Gospodarowicz MK et al. (2017).

to reflect the improved prognosis of these cancers: only a size over 6 cm is used, the presence of multiple ipsilateral nodal metastases is classified as N1 disease, and ENE is excluded. For nasopharyngeal carcinoma, 6 cm is also the only size criterion used, and nodal involvement below the lower margin of the cricoid cartilage increases the stage. Retropharyngeal nodes are regarded as unilateral for the purposes of TNM staging. Clinical N staging differs from pathological N staging (not shown).

Treatment of metastatic neck nodes

The treatment options for cervical nodes in SCC include radiotherapy, nowadays delivered as intensity-modulated therapy, with or without adjuvant chemotheraphy, and/or oncological surgical procedures termed neck dissections. The choice between definitive surgery and chemoradiotherapy for the neck depends on several factors but is guided by the treatment of the primary site. Neck dissections are oncological procedures to remove positive or at-risk neck nodal groups. A radical neck dissection entails unilateral en bloc removal of the neck lymph nodes from levels I to V on one side, as well as the ipsilateral sternocleidomastoid muscle, internal jugular vein, submandibular gland, and spinal accessory nerve. Modified radical neck dissections are much more commonly performed and are similar except that they preserve one or more of the aforementioned non-lymphatic structures to reduce long-term complications, e.g. sparing the spinal accessory nerve to prevent a frozen shoulder. These are undertaken for clinical node-positive necks without adverse features. A selective or functional neck dissection is a procedure in which one or more nodal groups are preserved. This is indicated as an ‘elective’ procedure in patients with no clinical (including radiological) evidence of nodal metastases (N0 necks) but sufficiently high risk of occult nodal metastases (risk estimated to be 20% or higher), which includes most SCC sites except low-T stage glottic cancers and some low-stage oral cancers. It may also be performed ‘therapeutically’ for some small primary cancers with small nodal disease (N1). An example of this is a supraomohyoid neck dissection, which includes removal of nodal levels I–III and is commonly performed electively for low-stage oral cancers. Neck dissections may be followed by postoperative chemoradiotherapy if adverse histological features are found, including extranodal extension or microscopically involved margins (66).

Head and neck SCCs with an unknown primary

Five percent to 10% of SCCs present with neck nodal metastases where the primary site is clinically not apparent; 90% of these arise in the palatine tonsil or tongue base, with the remainder mostly arising in the piriform sinus and nasopharynx (67). Most of these cancers are detectable on cross-sectional imaging, although a proportion are obscured by lymphoid tissue in Waldeyer’s ring. PET-CT is indicated if CT or MRI is negative or equivocal, as it can disclose the primary tumour as an asymmetrical focus of increased FDG uptake in up to one-third of cases (Figure 1.32). A small percentage of pharyngeal cancers are occult on all imaging modalities and only detected pathologically following extensive work-up including diagnostic biopsies, tonsillectomies, and a mucosectomy of high-risk sites. A true carcinoma of unknown primary (CUP) in the
Tumours of the oral cavity and pharynx

A cervical lymphadenopathy is defined as the primary tumour that is not detected after exhaustive search on imaging, which includes cross-sectional imaging and PET-CT, clinical assessment, and surgical biopsies of all high-risk sites (Figure 1.30). These are relatively rare (1%–2%) and are declining because of better detection methods (68). True CUPs probably reflect microscopic primary cancers that have been missed on pathological sectioning of surgical specimens or have regressed spontaneously. In the eighth edition of TNM staging, CUPs are staged differently according to the HPV and EBV status of metastatic nodes, reflecting their different prognoses and management (e.g. radiation portals), as follows: HPV/P16 positive, N staging as for HPV-positive oropharyngeal SCC; EBV positive, N staging as for EBV-positive nasopharyngeal cancer; HPV/EBV negative, N staging as for HPV-negative oropharyngeal SCC (28) (Figure 1.30).

**Key points: Cervical lymphadenopathy**

- Radiological evaluation of neck nodes is far more accurate than palpation, but both false-positive and false-negative results on imaging can occur.
- Ultrasonography with FNAC, MRI-DWI, and FDG PET can improve detection of nodal metastases but also have limitations, and no imaging modality can detect micrometastases.
- Anatomical radiological criteria used in nodal staging are nodal location, multiplicity, size, necrosis, and extranodal extension (ENE).
- Undifferentiated nasopharyngeal carcinoma has markedly different N staging compared with other head and neck cancers.
- HPV/P16 status of SCCs in the oropharynx profoundly influences N staging.
- Clinical ENE refers to clinical evidence of ENE, which may be supported by radiological findings.
- N staging of head and neck carcinomas of unknown primaries is subdivided into three groups depending on their EBV and HPV status.

**DISTANT METASTASES AND SECOND PRIMARY TUMOURS**

Distant metastases are a major determinant of prognosis and survival. The reported incidence of distant metastases is between 5% and 17% (69). The lungs are the commonest site involved (70%–85%), followed by bone (15%–39%) and liver (10%–30%) (69). Factors associated with an increased risk include hypopharyngeal location, advanced locoregional stage at presentation (T3/T4, N2c/N3), low jugular or supraclavicular fossa nodal involvement, ENE, and locoregional recurrence (70,71). Pathological risk factors also include unfavourable histology (e.g. adenoid cystic carcinoma), low histological grade, perineural or vascular invasion, and neo-angiogenesis (72).

Screening for distant metastases needs to be balanced against costs including financial and psychological burden associated with work-up of incidental findings. In high-risk patients, a whole body FDG PET-CT is performed, which has an overall sensitivity of 89% and a specificity of 95% (73). In lower-risk patients, a CT chest is cost effective and accurate to stage the chest and detect synchronous lung primaries, and includes other at-risk sites including the liver, adrenals, and the upper skeleton. CT thorax has replaced chest radiographs for this indication due to its superior sensitivity (74,75).

In head and neck cancer patients, the prevalence of synchronous tumours is 1%–6% (76), and the annual incidence of metachronous cancers, defined as developing 6 or more months following an index head and neck cancer, is estimated to be 3.8%. Approximately 40% of second primaries are located in the head and neck, followed by lungs (30%), oesophagus (8%), and other sites.

![Figure 1.32](image_url) Axial CECT (a) and PET-CT (b) in a patient with metastatic right upper jugular nodes from a squamous cell carcinoma on cytology (white arrows). The primary tumour was not identified clinically. On CT, (a) there is subtle mild mucosal asymmetry along the right lateral oropharyngeal wall posterior to the tongue base (arrowhead). This was deemed equivocal and thus a PET-CT was performed (b), which shows mild asymmetrical mucosal uptake posterior to the right tongue base. This site was selectively included in a subsequent panendoscopy and biopsy of at-risk sites, which confirmed SCC.
(e.g. colon, stomach, bladder), which is consistent with the field cancerization model \((77,78)\). They are less common in patients with HPV-driven cancers who lack other risk factors \((76,79)\)

**Key point: Distant metastases and second primary tumours**

- The need for extensive imaging to identify metastatic disease depends on consideration of tumour histology, site, and stage.
- Nasopharyngeal and adenoid cystic carcinomas have an increased risk of developing distant metastases.
- There is an increased incidence of second primary tumours.

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**POST-THERAPEUTIC IMAGING**

**Tissue changes after radiotherapy**

After irradiation of a neck cancer, alterations in surrounding tissues occur that are visible on imaging \((80,81)\). These expected alterations, which depend on dose rate, irradiated volume, and time elapsed, should not be confused with cancer. Mucositis is a common early finding, appearing as diffuse mucosal thickening and oedema on CT and MRI, usually with higher T2 signal than tumour and moderate post-contrast enhancement. Other changes include thickening of the skin and platysma muscle, reticulation of adipose in subcutaneous and deep tissue layers, laryngeal and retropharyngeal oedema, and altered signal of the major salivary glands.

Chronic post-radiation changes include atrophy of the salivary glands, lymph nodes, and lymphoid tissue; chronic thickening of the skin; signal alterations; and atrophy of muscles including the platysma, pterygoid, and constrictor muscles (Figure 1.33). Changes usually appear symmetrical unless asymmetric radiation portals were used. Most post-radiation changes stabilize by 18 months, although scar tissue may mature over years and typically appears T2 hypointense with minimal post-contrast enhancement.

**Tissue changes after surgery**

Besides neck dissections, which have been described earlier, surgical reconstructions are commonly used in head and neck patients. Flaps may comprise skin, fascia, muscle, and bone; these are local if transferred geometrically from adjacent tissue, pedicled if harvested on a paddle that is rotated to cover a defect while preserving the original blood supply, or free flaps if tissues are Anastomosed to the recipient site using microvascular techniques. A musculocutaneous pedicled flap using the pectoralis major is widely used to fill sizeable defects after laryngopharyngectomy and for recipient sites that are poorly vascularized because of previous irradiation. On imaging, this flap appears initially as a bulky soft tissue structure with characteristics of muscle. Gradually, denervation atrophy develops, causing volume loss and fatty replacement of the muscle (Figure 1.34). Muscle denervation may be incomplete at the time of imaging; fibre-like structures with muscle density within the flap should not be confused with tumour recurrence. The radial forearm free flap provides modest bulk and has a thin and pliable skin paddle, making it one of the most popular flaps for defects in the oral cavity and pharynx. Other free flaps include rectus abdominis myocutaneous, lateral arm, anterior lateral thigh, iliac crest, fibula free flaps (often used for mandibular reconstructions) and jejunal

---

**Figure 1.33** (a) Patient with a right-sided T2 piriform sinus cancer, before radiotherapy. The enhancing soft tissue thickening on the right aryepiglottic fold corresponds with the tumour (arrow). (b) Anatomically corresponding image, 6 months after radiotherapy. Thickening of the infrahyoid epiglottis (arrow), as well as pronounced and symmetric thickening and increased attenuation of the aryepiglottic folds is seen (asterisks). Note also the thickening of the hypopharyngeal walls (black arrowheads) and the retropharyngeal oedema (white dots). Also, slight thickening of the platysma muscles is seen (white arrowheads).
free flaps (sometimes used to reconstruct the pharynx after total laryngopharyngectomy) (82). Flaps can show variable T2 signal and enhancement; the latter usually diminishes over time.

**Post-treatment imaging**

No imaging is required for patients with early-stage disease that is definitively treated and can be assessed easily clinically. For the remainder, an initial follow-up CT or MRI may be performed between 3 and 6 months after surgery, radiotherapy, or combined treatment. This timeframe allows transient inflammatory changes that distort the anatomy and hamper imaging interpretation to subside sufficiently; furthermore, anatomical changes including regression of primary tumours and metastatic nodes that have been successfully treated by chemoradiotherapy may only be evident by this time. Post-treatment imaging is used to identify residual disease and document the post-treatment appearances, thereby serving as a baseline. By comparing subsequent imaging studies with the baseline study, detection of residual or recurrent disease, as well as treatment-related complications, is possible with greater confidence and at an earlier stage than with clinical follow-up alone (Figures 1.35 and 1.36).

The baseline study itself carries important predictive information regarding the eventual local outcome. For example, reports suggest that CT may be used for early differentiation of treatment responders from non-responders in irradiated laryngeal and hypopharyngeal cancer (83,84).

Based on the appearance of the larynx/hypopharynx on an early post-radiotherapy CT study, a prediction of long-term local outcome can be made according to the following scores:

- **1** = Expected post-radiotherapy changes, i.e. complete resolution of the tumour at the primary site and symmetrically appearing laryngeal and hypopharyngeal tissues, as described earlier
- **2** = Focal mass with a maximal diameter of <1 cm and/or asymmetric obliteration of laryngeal tissue planes
- **3** = Focal mass with a maximal diameter of >1 cm or <50% estimated tumour volume reduction (84,85)
Post-therapeutic imaging

The post-radiotherapy CT score 1 was shown to be a very strong predictor of long-term local control; patients with such findings on post-radiotherapy CT will probably not benefit from further follow-up imaging studies. Conversely, patients with a first follow-up examination classified as a CT score 3 do very poorly; almost all these patients will develop a local failure (85). Further exploration in such post-radiotherapy CT score 3 patients is warranted. FDG PET-CT is a useful intermediate step in cases where biopsy is considered too risky or if a biopsy result is returned as negative. Indeed, the predictive value of a negative biopsy for local control is reported to be only 70% (86). This is likely due to sampling error, as tumour recurrences initially develop submucosally and can therefore not be accurately targeted. If there is discrepancy among clinical findings, CT findings, results of radionuclide studies, and/or biopsy, close clinical follow-up and repeat imaging studies are indicated.

The local outcome of patients initially classified as post-radiotherapy CT score 2 is indeterminate. Unless clinical examination is already suspect for local failure, further follow-up CT studies are needed in these patients; a time interval of 3–4 months is recommended, to be continued up to 2 years after completion of radiation treatment (Figure 1.25).

MRI is also of value for post-treatment assessment. Residual tumours tend to appear as expansile masses with intermediate T2 signal (between muscle and cerebrospinal fluid [CSF]) and intermediate enhancement. Furthermore, residual masses that are retracted or have flattened edges and display low T2W signal throughout usually represent fibrotic scar tissue and have a very low risk of recurrence (Figure 1.37) (87). DWI may also be useful as tumours responding to irradiation show a rise in diffusion and a rise in ADC (88–90). Some reports suggest a low ADC, e.g. less than 1.2 × 10⁻³ mm², in the primary site or nodes post-treatment is accurate for residual or recurrent tumour (89–91).

Post-treatment assessment with PET-CT is increasingly being used first line to assess response of advanced head and neck cancers after definitive chemoradiotherapy. If performed between 9 and 12 weeks after completion of treatment, the negative predictive value of PET-CT is over 97%, which may be used to avoid further interventions in patients displaying both a complete metabolic and anatomic response (92–94). Nevertheless, the positive predictive value of PET-CT is suboptimal during this time frame, mainly because of increased metabolic uptake by radiation-induced inflammation, although this improves over time. Consequently, any metabolically positive findings must be interpreted cautiously (95,96). PET-CT may be particularly useful for patients with advanced nodal disease (N2b/N3) from SCC treated by (chemo)radiotherapy as these patients often have indeterminate residual nodal masses on initial post-treatment cross-sectional imaging, although most will not develop regional recurrences (Figure 1.38). Historically, post-radiotherapy neck dissections were advocated for this subgroup to optimize the chances of regional cure and survival, although, as only a quarter of neck dissection specimens were pathologically positive (97), this strategy subjected most patients to potentially avoidable surgeries and complications. Fortunately for this subgroup, a negative neck on PET-CT performed around 12 weeks post-treatment is highly predictive of a complete regional response, and a recent randomized clinical trial has suggested that a ‘watch and wait strategy’ of neck monitoring based on negative PET-CT achieves equivalent survival to a planned neck dissection but with lower morbidity and higher cost effectiveness (98).

Figure 1.36 Patient treated by irradiation for a right-sided T3 piriform sinus cancer. (a) Axial CECT obtained 6 months after completion of therapy. Clinically, there is no evidence of disease. Subtle asymmetry of the right hypopharyngeal tissues is visible (arrows) is present, which was thought to be intermediate risk, and a follow-up CT study was recommended. (b) Axial CECT obtained 4 months later. Clinically, there was no evidence of disease. There is now a nodular inhomogeneously enhancing submucosal mass in the right piriform sinus apex/postcricoid hypopharynx, which is highly suspicious for recurrence. Endoscopic biopsy revealed carcinoma.

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Although these results are promising, more evidence is required with respect to subgroup stratification, notably for patients with very bulky nodal metastases (N3). The optimal management for patients with residual nodal abnormalities on CT that display no metabolic uptake on PET is presently unclear.

Long-term surveillance

Approximately one-quarter of head and neck cancer patients develop a recurrence, most of which occur within 2 years (90%) (99). These are more commonly local or regional although distant failures are increasing in relative frequency. Head and cancer patients usually have frequent clinical follow-up for at least 2 years post-treatment (100), although there is no consensus regarding repeated imaging after the baseline scan. Nevertheless, patients with advanced or clinically inaccessible tumours may undergo CT or MRI at 3–6 month intervals for the first 2 years and thereafter depending on continued risk. Other techniques including PET-CT and US combined with FNAC may also be used selectively. Recurrences typically arise within the original primary bed or previously metastatic

Figure 1.37  Patient treated by irradiation for a right-sided oropharyngeal carcinoma. (a) Axial T2W MRI pretreatment showing a bulky right tonsillar tumour (black arrow) extending across the glossotonsillar sulcus into the base of tongue (black arrowhead). (b) Axial T2W MRI 6 months after radiation therapy showing there is a focal nodule <1 cm (white arrow) and diffuse thickening along the right constrictor muscle (white arrowheads), both of which are markedly T2 hypointense suggestive of scar tissue. There was no recurrence clinically as of 3 years after end of treatment.

Figure 1.38  Patient with T4aN2c oropharyngeal cancer: (a) Axial CECT image obtained before therapy shows centrally necrotic adenopathy in level III on left side (arrows). (b) CT image obtained 2 months after end of chemoradiotherapy. The primary tumour (not shown) responded well to treatment. The adenopathy (arrows) is only slightly diminished in size (diameter at that time about 1.4 cm). In this patient, a wait-and-see policy was adopted; no neck dissection was performed. The adenopathy gradually decreased in size on follow-up CT studies. There was no evidence of disease 4 years after end of treatment.
nodes, although marginal recurrences can also occur. Recurrences may also present as delayed complications such as fistulae and tissue necrosis. There is no agreement regarding imaging surveillance for metachronous cancers and distant metastases although annual chest radiographs or low-dose CTs may be considered for high-risk patients.

**Treatment complications**

**Complications after surgery**

Most surgical complications occur early after treatment and are dealt with on a clinical basis. Imaging may be required in the assessment of haematomas, chylous and serous collections, abscesses, flap dehiscence and necrosis, and fistulae involving the oral cavity and pharynx. The development of complications including fistulae after an initially normal postoperative recovery interval should raise the possibility of tumour recurrence.

**Complications after radiotherapy**

Acute radiotherapy effects including mucositis and skin desquamation usually settle spontaneously. Necrosis of soft tissue, cartilage, and bone is rare after radiotherapy, usually appearing after months or years. Osteoradionecrosis can involve the mandible, larynx, skull base, temporal bone, and the hyoid bone (Figure 1.39) (101, 102). Mandibular osteoradionecrosis is exacerbated by dental surgery, extraction, biopsy, or dental caries. Radiological findings include bony sclerosis, cortical and cancellous destruction, sequestrations, pathological fractures, soft tissue thickening, and fistula formation. Thickening and contrast enhancement of adjacent soft tissues can be prominent such that differentiating osteoradionecrosis from recurrence may be challenging. Furthermore,

**Figure 1.39** Patient treated 5 years earlier for left-sided oral cavity cancer, by surgery and postoperative external radiotherapy. The patient suffered oral ulceration and pain for several months and presented with more pronounced symptoms and soft tissue swelling. CT (bone window) shows osteolytic changes in the mandibular symphysis and left body, complicated by a pathological fracture (between arrowheads). Bone sequesters are seen (arrows), as well as some intraosseous gas bubbles. The perimandibular soft tissue appears to be swollen. There is contralateral bone defect (asterisk). Mandibular osteoradionecrosis was diagnosed.

**Figure 1.40** Patient irradiated for right-sided tonsillar cancer. The patient suffers from persisting pain in this region; clinically, an ulceration is visible. (a) Follow-up axial CECT, obtained about 18 months after the completion of irradiation, shows soft tissue ulceration, with some surrounding soft tissue infiltration and slightly increased enhancement (arrowheads); this was reported as possibly reflecting recurrent tumour. Biopsies were negative for cancer, but an additional FDG PET (b) study showed focal tracer uptake at the same level (arrows), reported to be suspicious for tumour recurrence. A partial oropharyngectomy, including resection of the adjacent part of the mandible was performed. The resection specimen showed soft tissue inflammatory changes and radionecrosis but no evidence of malignancy.
patients may also develop osteomyelitis, which adds to the diagnostic confusion. In the mandible, extensive bony sclerosis, as well as cortical defects positioned away from the original tumour, suggests osteoradionecrosis, whereas an asymmetric, discrete, solid, enhancing mass suggests recurrence (102). PET-CT is unhelpful for problem solving as both osteonecrosis and recurrence are FDG avid (103). Chondronecrosis of the laryngeal skeleton can occur following radiotherapy for hypopharyngeal cancers, which may be indistinguishable from recurrence, although presence of gas around the cartilage is suggestive of necrosis (104). It has been suggested that FDG PET-CT may allow differentiation between tumour recurrence and tissue necrosis after therapy, although false-positive results are common because tissue necrosis and inflammation usually coexist (Figure 1.40) (105,106).

Radiotherapy-induced fibrosis can produce substantial morbidity, including aspiration due to pharyngeal and laryngeal dysfunction, dysphagia due to pharyngeal stenosis, and restricted mouth opening due to masticator muscle fibrosis. Radiological features of fibrosis can overlap with tumour including in terms of enhancement, such that follow-up studies are often needed to rule out recurrence with a sufficient degree of confidence. Other chronic complications of radiotherapy include arteriopathy, radiation injury of the brain (white and grey matter injury, necrosis, and cysts), radiation myelopathy, cranial nerve palsy, glandular injury, granulomatous polyps, and radiation-induced tumours, notably squamous cell carcinoma and sarcoma.

### SUMMARY

- Most malignant tumours of the oral cavity and pharynx are SCCs.
- Imaging is essential in defining local extent, lymph node involvement, and distant metastasis.
- Head and neck cancer is not a single disease. Each site in the head and neck has its own characteristics regarding locoregional cancer behaviour, response to treatment, and risk for recurrent disease.
- Perineural tumour spread can be silent, thus its detection by imaging is essential to avoid undertreatment and persistent/recurrent cancer.
- Subclinical adenopathies may be detected by imaging studies; particular attention should be paid to clinically inaccessible nodal sites such as retropharyngeal and paratracheal nodes.
- It is essential to know what to expect on imaging studies after radiotherapy and/or surgery, so that these changes are not misinterpreted as evidence for cancer recurrence. Conversely, care should be taken not to misinterpret recurrent cancer as post-treatment changes; biopsy, a repeat CT/MRI after a short interval, or a PET-CT study may be appropriate.
- Baseline post-treatment imaging and imaging surveillance in high-risk patients allows identification of recurrent cancer earlier than clinical examination in a substantial number of patients.
- Tissue necrosis after radiotherapy may be difficult to differentiate from recurrent tumour, although there are imaging features suggestive of each.
- Biopsy results may be false negative initially in cases of recurrent tumour. In case of discrepancy between clinical, imaging, and/or biopsy findings, close follow-up and repeat imaging studies are needed.

### Key points: Imaging after treatment

- Irradiation produces expected tissue changes on post-treatment imaging studies, which should not be misinterpreted as evidence of persistent or recurrent disease.
- Expected changes after radiotherapy appear symmetric, unless the neck was irradiated using asymmetric radiation portals.
- Early imaging identification of recurrent tumour is facilitated by obtaining a baseline study about 3–6 months after therapy.

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