The Royal College of Pathologists
Pathology: the science behind the cure

Standards and Datasets for Reporting Cancers

Datasets for histopathology reports on head and neck carcinomas and salivary neoplasms (2nd edition)

June 2005

This dataset was commissioned by The Royal College of Pathologists' Working Group on Cancer Services. It replaces the first edition published in 1998.

According to the College's pre-publication policy, this document was placed on the College website for consultation from 16 November to 12 December 2004. Five pieces of feedback were received, which were forwarded to the lead author and considered in this final version.

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Director of Publications

Acknowledgement

The Royal College of Pathologists' Working Group on Cancer Services acknowledges the use of the *Appraisal Instrument for Clinical Guidelines* (Cluzeau F, Littlejohns P, Grimshaw J, Feder G. London: St George's Hospital Medical School, May 1997) in the preparation of this publication.

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General introduction to the *Standards and Datasets for Reporting Cancers*

All these documents are evidence-based and define the minimum standards for reporting each group of tumours. They conform to a standard format and include a proforma that is intended to function as an *aide memoire* when reporting specific tumours. Although the data in the proforma may be presented as or supplemented by free text, the use of proformas in histopathological reporting is recommended; published audits have shown that they are very effective in ensuring that all necessary data are provided.[1,2]

Copies of the reporting forms are available at the end of this booklet and can also be downloaded from the College website (www.rcpath.org/publications).

Recommendations

The Royal College of Pathologists' Working Group on Cancer Services recommends that:

- the datasets for reporting tumours are used in the system of standard setting, data collection, audit and feedback for those involved in caring for these patients
- histopathology laboratories nominate a lead pathologist for each of the main cancers with responsibility for liaising with relevant local committees and clinicians and ensuring that the relevant cancers are examined, sampled and reported appropriately and in a consistent fashion
- histopathologists should be members of multidisciplinary teams dedicated to the diagnosis and management of patients with specific cancers (and be involved in auditing the service)
- the SNOMED coding system is used to achieve as much uniformity as possible from centre to centre and to facilitate reliable cancer registration. Either the 1979 or 1993 version of SNOMED can be used, as currently there is no clear consensus for using one or the other
- histopathologists reporting cancers should participate in appropriate external quality assessment (EQA) schemes
- Cancer Centres and Units should be supported only by laboratories accredited with CPA (UK) Ltd and staffed in accordance with the recommendations of The Royal College of Pathologists and the Association of Clinical Pathologists.

Feedback

Anyone wishing to make specific or general comments on any of the documents should contact Dr Timothy Helliwell, Department of Pathology, University of Liverpool, Duncan Building, Daulby Street, Liverpool, L69 3GA. Email: trh@liv.ac.uk

This document will be reviewed if new evidence emerges.

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References

1. Cross SS, Angel CA. Five audit cycles of the informational content of histopathological reports of bladder carcinoma. *J Pathol* 1997;181:7A.
2. Cross SS, Feeley KM, Angel CA. The effect of four interventions on the informational content of histopathology reports of resected colorectal carcinomas. *J Clin Pathol* 1998; 51:481–482.

Datasets for histopathology reports on head and neck carcinomas and salivary neoplasms (2nd edition)

Coordinators: Dr TR Helliwell and Dr JA Woolgar, University of Liverpool

GENERAL OVERVIEW

These guidelines present the core data that should be provided in histopathology reports of specimens of squamous carcinomas originating in the mouth, nose, pharynx and larynx, malignant neoplasms arising in the major salivary glands, and neck dissection specimens for metastatic disease. The datasets for squamous carcinoma and neck dissections are unchanged since the first edition of this publication, but the guidelines have been revised in the light of a national audit in 2001 and more recent evidence supporting the inclusion of specific data items. The appendices list current systems of classification and staging for these malignancies, as well as illustrative histopathology request forms and proforma reports.

The guidelines should be implemented for the following reasons.

1. Certain features of invasive mucosal carcinomas (type, size and grade of the primary carcinoma, the pattern of invasion and proximity of carcinoma to resection margins, lymph node status and the presence of extranodal spread) have been shown to be related to clinical outcome.[1–8] Similar principles apply to salivary malignancies.[9–11] These features may therefore be important in:
   a) deciding on the most appropriate treatment for particular patients, including the extent of surgery and the use and choice of adjuvant radiotherapy or chemotherapy
   b) monitoring changing patterns of disease, particularly by cancer registries.
2. These features provide sufficiently accurate pathological information that can be used, together with clinical data, for the patient to be given a prognosis.
3. To allow the accurate and equitable comparison of surgeons in different surgical units, to identify good surgical practice and the comparison of patients in clinical trials.

The criteria have been widely discussed by pathologists and surgeons, and formal approval was sought from the British Society of Oral and Maxillofacial Pathology, the British Association of Head and Neck Oncologists, the British Association of Oral and Maxillofacial Surgeons, the British Association of Otolaryngology – Head and Neck Surgeons, the UK Association of Cancer Registries. Comments from specialist and general histopathologists on the draft version of this document, which was published for consultation on the College website in 2004, have been considered as part of this dataset.

On the request forms, we are grateful to Professor DG McDonald, University of Glasgow, for permission to use the diagrams of the oral cavity and jaws, and to the International Union Against Cancer (UICC) and Springer-Verlag to use the diagrams of the larynx and neck that are adapted from the *TNM Atlas (3rd edition)*, 1989.

Section A Mucosal malignancies of the head and neck region

This section applies to the reporting of squamous carcinomas of the upper aerodigestive tract, i.e. those arising in the nose and paranasal sinuses, mouth (including the tongue), pharynx (including nasopharynx, hypopharynx, oropharynx and tonsillar area) and larynx. Squamous carcinoma accounts for 95% of malignant neoplasms arising at these sites, but similar principles may be applied to the reporting of other mucosal malignancies arising in this anatomical area including adenocarcinomas, undifferentiated nasopharyngeal carcinomas, malignant melanoma, and to neuroendocrine epithelial neoplasms including carcinoid tumour, small cell carcinoma and olfactory neuroblastoma, that are important considerations in the differential diagnosis but are not described in detail.

Optimal reporting of specimens from the head and neck area requires a partnership between the pathologist and surgeon/oncologist. The surgeon can help the pathologist to provide the information necessary for patient management by the appropriate handling and labelling of the specimen in the operating theatre. Regular discussion of cases at clinicopathological meetings and correlation with pre-operative imaging studies are important in maintaining and developing this partnership.[12]

The guidelines are presented as a proforma that lists the core data items that may be applied across the head and neck region. The proforma may be used as the main reporting format or may be combined with free text as required. Individual centres may wish to expand the detail in some sections, e.g. for sites and subsites, to facilitate the recording of data for particular tumour types.

A detailed dissection protocol is beyond the scope of these guidelines, but a brief summary of dissection methods and block selection is included to facilitate recording of the core data items.

SPECIMEN REQUEST FORM

The request form should include patient demographic data, the duration of symptoms, whether surgery is palliative or curative, details of previous histology or pathology reports and the core clinical data items (see below). Clinical TNM stage is useful as the final pathological T coding at some sites, e.g. the larynx, will be determined by clinical features such as vocal cord mobility.[13] A history of previous radiotherapy or chemotherapy should be included, as this may influence the interpretation of the histological changes and should prompt a comment on the extent of any response to treatment. The request form should provide the opportunity for surgeons to provide annotated diagrams of specimens either as free-hand drawings or on standard diagrams (see Appendix D). Copies of reports that are sent to the Cancer Registries should include the patient's address if possible.

PREPARATION OF THE SPECIMEN BEFORE DISSECTION

Resection specimens should be orientated by the surgeon and pinned or sutured to cork or polystyrene blocks. The surgeon should indicate surgically critical margins using metal tags or sutures. Fixation is in a formaldehyde-based solution for 24–48 hours in a container of adequate size (the volume of fixative should be ten times that of the tissue).

Photography and radiography of the specimen may be used to record the nature of the disease and the sites from which tissue blocks are selected. Surgical margins should be painted with Indian ink or an appropriate dye to facilitate the later recording of the proximity of carcinoma to the margin.

NOTES ON SITE-SPECIFIC CONSIDERATIONS AND BLOCK SELECTION

Oral cavity and oropharynx

In general, these specimens may be assessed by cutting the specimen with a large knife into 5 mm slices to demonstrate both the relationship of the tumour to mucosal resection margins and the maximum depth of invasion by the tumour. Specimens from the central and lateral parts of the mouth should be cut in the coronal plane, while specimens from the anterior mouth should be sliced in the sagittal plane. If the tumour is close to bone, the specimen should be decalcified with soft tissue *in situ*.

Larynx and hypopharynx

5 mm thick horizontal slices provide optimal demonstration of the relationship between the tumour and the laryngeal cartilages. For supraglottic carcinomas, blocks should include the relationship between the carcinoma and the anterior (submucosal) resection margin at the base of the tongue; blocks taken in the sagittal plane are more appropriate to demonstrate this feature. The description should include the subsite of origin of carcinoma, and the extent of involvement of laryngeal cartilages and extra-laryngeal tissues.[14]

Paranasal sinuses and maxillectomy specimens

These are complex specimens that require careful orientation and labelling by the surgeon if the pathologist is to provide accurate information. When appropriate, the surgeon should assist the pathologist in the dissection of the intact specimen to ensure that critical margins are oriented and submitted for histological examination. For partly disrupted specimens, it may sometimes be necessary for surgically critical margins to be sent as separate specimens to the laboratory.

Selection of blocks for histology

- Tumour – at least one block per 10 mm diameter of tumour, including one selected to demonstrate the maximum depth of invasion; whole tumour if less than 10 mm.
- Blocks of defined mucosal and soft tissue margins.
- Non-neoplastic mucosa.
- Bone surgical margins (if applicable).
- Bone or cartilage (larynx, nose), if grossly involved by tumour.
- Thyroid if present in laryngectomy.
- Tracheostomy site.

CORE DATA ITEMS TO BE INCLUDED IN THE HISTOPATHOLOGY REPORT

1 Clinical data (provided by the surgeon or oncologist)

1.1 Site(s) and side(s) of the carcinoma(s). For carcinomas that involve more than one site, the principal site of involvement should be recorded and coded; this may not be the site of origin. If required, the involvement of associated sites can be noted to help in later data analysis. Sites and subsites should be recorded according to the International Union Against Cancer (UICC) nomenclature (see Appendix A).

1.2 Type of resection specimen, e.g. total or partial glossectomy, laryngectomy.

2 Pathological data

2.1 Maximum diameter of tumour (in millimetres). The macroscopic diameter should be used (Figure 1) unless the histological extent is greater than macroscopically apparent, in which case the microscopic dimension is used. As for other tissues, e.g. breast, measurements are made pragmatically, acknowledging distortion of tissues by fixation and processing.

2.2 Maximum depth of invasion (millimetres) below the luminal aspect of surface; if the tumour has ulcerated then the reconstructed surface should be used (Figure 1). The aim should be to provide a best estimate of tumour depth; for large carcinomas this may be an approximation. A more detailed comment on the nature of the tissues invaded (mucosa, muscle, etc.) should occur in the 'Comments' sections. Tumour thickness is significantly related to nodal metastasis, although the optimal cut-off point for prognostic purposes is uncertain, with 3 mm and 5 mm being suggested by different studies of lingual carcinomas.[15, 16]

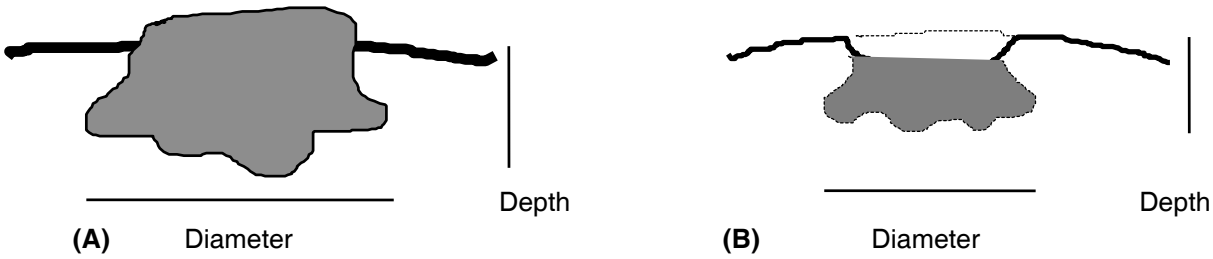

Figure 1 Descriptors of the size of the primary carcinoma. (A) for a nodular carcinoma and (B) for an ulcerated carcinoma. Note that depth of invasion refers to the depth of greatest spread in presumed continuity below the top of the adjacent mucosa. For both nodular and ulcerated tumours, the line of the original mucosal surface is reconstructed to determine the true thickness.

2.3 Histological type of carcinoma. These guidelines specifically apply to conventional squamous carcinomas. Subtypes of squamous carcinoma, such as papillary, verrucous, basaloid, adenosquamous and spindle cell carcinomas, should be recognised[17] and listed in the core dataset and potential prognostic implications noted in the 'Comments' sections.

2.4 Degree of differentiation. Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the World Health Organization (WHO) classification.[17] The most aggressive area (medium magnification field) is graded as well differentiated, moderately differentiated or poorly differentiated. This system is widely used and prognostically useful, even though it suffers from inter-observer variability and sampling problems.[5,18] While most squamous carcinomas will be moderately differentiated, it is important for prognostication to separate well differentiated and poorly differentiated tumours.

2.5 Invasive front of the carcinoma. The pattern of invasion by the carcinoma at its deep margin is of proven prognostic value for oral carcinomas.[4,19,20] The few published studies of tumours at other sites suggest that a similar approach may be of value.[3]

Scoring systems for histopathological features of squamous carcinomas include features related to differentiation and to the tumour/stromal interaction.[1–3] While these have the potential to improve the consistency of reporting, they are not in widespread use and for these guidelines it is suggested that the recording of differentiation and invasive pattern is made separately.

It should be recognised that the pattern of tissue invasion by carcinoma is a continuous spectrum of changes. For prognostic purposes, two groups can be recognised: carcinomas composed of broad cohesive sheets of cells or strands of cells (more than 15 cells across), and carcinomas composed of narrow strands, non-cohesive small groups or single cells (see Figure 2).[4]

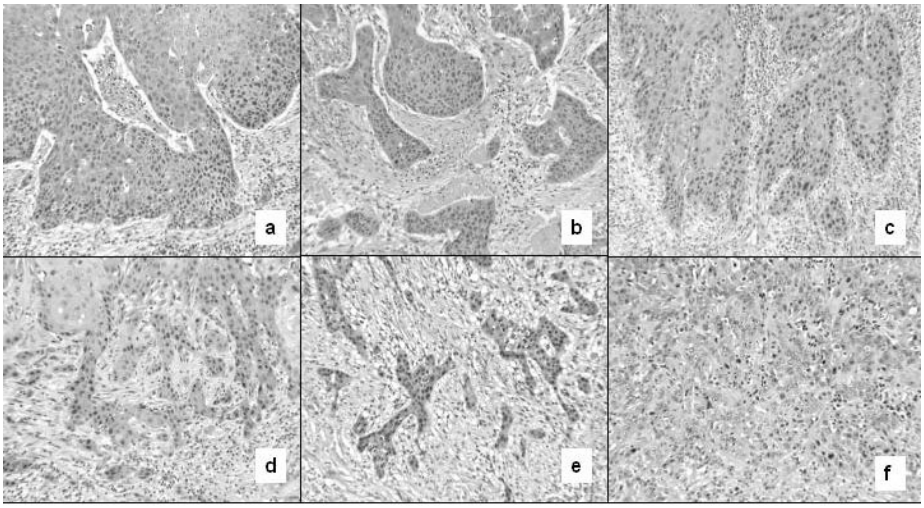

Figure 2 Patterns of invasion by squamous carcinoma.
a, b, c are examples of cohesive patterns.
d, e, f are examples of non-cohesive or infiltrating patterns.

2.6 Distance from invasive carcinoma to surgical margins (in millimetres). Measure the distance histologically for both mucosal and deep margins. From a surgical point of view, >5 mm is 'clear', 1–5 mm is 'close' and <1 mm is 'involved'. Incomplete resection or the presence of dysplasia at the margin is associated with a significantly increased risk of local recurrence.[21] In the 'Comments' section, it may be noted that if the tumour has an infiltrating pattern of invasive front (or vascular or perineural spread ahead of the invasive front) and a close margin, this may be associated with a high risk of local recurrence. Note that comment on the deep resection margin of a laryngectomy specimen may be inappropriate unless the tumour extends close to the base of tongue or into the soft tissues of the neck.

2.7 Vascular invasion. The presence or absence of vascular invasion should be mentioned if it is an obvious feature on medium magnification examination of the tumour. The presence of carcinoma cells within an endothelial-lined space is the essential criterion. It is not necessary to distinguish between small lymphatics and venous channels.

2.8 Nerve invasion. The presence or absence of invasion of the perineural space ahead of the invasive front of the carcinoma should be recorded. This is especially important for carcinomas of the lip where this feature predicts local recurrence. Intra-tumoural perineural invasion is of doubtful prognostic significance.

2.9 Bone invasion or cartilage invasion. The involvement of bone may be by non-invasive erosion of the cortex, or diffuse infiltration of medullary intertrabecular and perineural tissues.[13] These should be distinguished in the 'Comments' section. If bone margins can be identified, the presence or absence of carcinoma at the margins should be described in the 'Comments' section.

2.10 Severe dysplasia/*in situ* carcinoma. Epithelial dysplasia forms a continuous spectrum of appearances from mild to severe dysplasia/carcinoma *in situ*. Detailed discussion of the criteria and reproducibility of grading systems is not part of these guidelines and consensus has not been reached on the most clinically appropriate and reproducible grading system. The options include the standard WHO system,[17] the system based on grades of squamous intraepithelial neoplasia[22] and the Ljubliana classification for laryngeal lesions.[23] Severe dysplasia and carcinoma *in situ* are generally regarded as synonymous and are associated with a high risk of progression to carcinoma. The presence of severe dysplasia/carcinoma *in situ* adjacent to the primary carcinoma and at the resection margins (where it may predict local recurrence) should be recorded.[24,25]

Other features form part of a complete description, but are not core data items

These features should be included as part of a comprehensive description of a carcinoma and the surrounding tissues. Some are preferences of individual centres, but are considered to be of uncertain prognostic significance at most sites in the head and neck region and therefore are not part of the dataset at present.

- Type and intensity of inflammatory infiltrate and desmoplastic stromal response.
- Involvement of a tracheostomy (if present).
- Response to previous therapy (if applicable).
- Results of other investigations, e.g. flow cytometry, molecular and immunohistochemical studies.

Molecular markers including measures of cell proliferation and nuclear DNA content, the expression of involucrin, blood group antigens, cell adhesion molecules and oncogenes, and the intensity of neoangiogenesis have been investigated as potential prognostic factors. These features generally correlate with cellular differentiation but do not provide any consistent independent prognostic information.[6,26,27] While molecular markers predictive of tumour behaviour or response to therapy may be required pathological data in the future, current surgical practice does not demand their inclusion in the dataset.[8,21]

Immunocytochemical studies may help to resolve differential diagnostic problems. Most antibodies lack a precise tissue or neoplastic specificity, so that a combination of appropriate results is required to make a diagnosis. These results should always be consistent with the haematoxylin and eosin appearances.

3 Diagnostic coding of primary carcinomas

3.1 pT status should be recorded according to the UICC guidelines (see Appendix A).[13]

3.2 SNOMED 'T' code(s) should be recorded for primary site(s). A list of 'T' codes against site and subsite is provided in Appendix B.

4 Reporting criteria for small biopsy specimens

4.1 The data that can be obtained from small biopsy specimens will be determined, in part, by their size. The type of carcinoma and its grade are the minimum data required to determine treatment. It is recognised that, in large tumours, the grade in superficial biopsy material may not be representative of the most aggressive part of the invasive front. If severe dysplasia/*in situ* carcinoma is present, this should be recorded as it may influence the position of excision margins. For larger diagnostic biopsies, as may be obtained from oral neoplasms, the pattern of invasion can be determined. It is not realistic to assess reliably the tumour thickness or presence of vascular invasion in small biopsies.

5 Use of frozen section diagnosis

5.1 The initial diagnosis of carcinoma will usually be made before definitive surgery is performed. On occasions, intra-operative frozen section diagnosis of the nature of a neoplasm will be required. While it will usually be possible to identify the presence of neoplastic tissue, the nature of a poorly differentiated neoplasm may be impossible to determine on frozen sections.

5.2 The assessment of the presence or absence of carcinoma at surgical resection margins is the most common indication for intra-operative frozen section diagnosis. The surgeon should select the tissue for frozen section diagnosis with care, bearing in mind that it is not usually possible to section material more than 10 mm in diameter.

5.3 The report on the frozen section specimen should form part of the final diagnostic report on the case.

Section B Salivary gland neoplasms

Malignant tumours of the salivary glands are usually removed by partial excision of the gland including the tumour mass, or by total excision of the gland. Parotid tumours may require an extended radical procedure with resection of the subcutis and skin of the pre/infra-auricular region and upper neck. Resection margins around salivary tumours will be either salivary tissue and/or soft tissue. The most important prognostic features are the histological tumour type, the clinical/pathological stage and the adequacy of the excision.[11,28]

The dataset does not cover benign salivary neoplasms, although pathology reports on these neoplasms would be expected to include an overall description of the specimen and the tumour, the histological type (WHO classification) and the proximity of the neoplasm to the resection margins.

The parotid gland is richly supplied with two networks of lymphatic vessels, paraglandular and intraglandular, which may or may not intercommunicate. Each gland contains 20–30 lymph nodes that may be the site of metastases from salivary tumours and other malignancies, particularly those arising in the head and neck region. The efferent lymphatics from the parotid drain primarily to the superior deep cervical nodes (level II). The submandibular gland does not contain intraglandular lymph nodes and the parenchyma drains to the 2–5 submandibular nodes that lie close to the gland, and then to nodes at level II. The sublingual gland drains to the submandibular, submental and level II nodes.[29]

SPECIMEN HANDLING AND BLOCK SELECTION

The exposed margin of the excised tissue should be marked with Indian ink or a suitable pigment before the tissue is serially sliced. If a major nerve has been resected, the proximal and distal margins should be indicated by the surgeon, thus facilitating accurate assessment of any peri- or intra-neural invasion.

Blocks to be taken

- Representative blocks of tumour (at least one per 10 mm of tissue diameter) to include normal tissue and the relationship between tumour and the nearest resection margin.
- Lymph nodes within the gland or in peri-glandular soft tissue.
- Blocks from designated resection margins of nerves.

Neck dissection specimens associated with salivary neoplasms are handled as described in Section C.

1 PATHOLOGICAL DATA

1.1 Macroscopic features

Core data items for a salivary tumour are:

- the maximum diameter of the tumour (in millimetres)
- the distance from the tumour to the nearest resection margin (the macroscopic measurements should be confirmed histologically and, if there is a discrepancy, then the histological distance should be stated in the dataset)
- macroscopic extraglandular extension to involve adjacent structures
- the histological type of neoplasm (according to the WHO classification)
- the grade of malignancy (see below)
- the presence or absence of perineural or vascular invasion
- the presence or absence of lymph node involvement.

1.2 Other macroscopic features form part of a complete description, but are not core data items:

- the type of specimen (superficial or total parotidectomy, extent of any neck dissection
- the overall size of the specimen with regard to anatomical features
- the length of the excretory duct, if obvious
- the size of the tumour in three dimensions
- a note of the presence and size of lymph nodes around or within the gland
- the nature of the tumour: solitary or multifocal; solid or cystic, etc.
- the nature of the edge of the tumour: discrete (well defined) or poorly defined
- the appearance and texture of the cut surface: translucent or cartilaginous, brown or haemorrhagic, cystic, necrotic, etc.

1.3 Other microscopic features form part of a complete description, but are not core data items:

- mitotic index
- microscopic encapsulation or invasion of normal tissues
- changes in the macroscopically normal salivary tissue
- immunocytochemical labelling may help to characterise some types of neoplasm that contain myoepithelial cells (e.g. caldesmon, calponin, p63, S-100 protein), luminal cell cytokeratins (CK 8, 18, 19) or mitochondria, but diagnosis should be based primarily on morphological criteria
- molecular markers such as MIB-1, bcl-2, p53, HER-2 may have prognostic value,[11, 30] but are not routinely performed.

2 DIAGNOSTIC CODING

2.1 pTNM stage according to standard criteria (see Appendix A). The TNM staging according to the UICC classification applies to tumours of the major salivary glands.[13] Salivary-type neoplasms of minor glands should be staged according to the criteria for mucosal squamous carcinomas.

2.2 SNOMED ‘T’ and ‘N’ codes (see Appendix B).

3 GRADING OF SALIVARY MALIGNANCIES

3.1 Mucoepidermoid carcinoma

Grading of mucoepidermoid carcinomas is related to metastatic potential and survival, whichever system is used.[9,31–33] In general, low-grade (cytologically benign) tumours with abundant mucous cells and mucin production are less aggressive and rarely metastasise. Tumours that are predominantly solid and have a preponderance of epidermoid cells have the greatest metastatic potential. There has been considerable debate around grading criteria and the relative merits of 2 and 3 grade systems. A modification of the American Forces Institute of Pathology (AFIP) grading system[31] has the merit of simplicity and appears to allow good discrimination between tumours with good and poor prognosis. This system scores a range of histological features but, in essence, the presence of two or more poor prognostic features indicates a high grade tumour (see Table 1).

Table 1 Prognostic features for mucoepidermoid carcinoma[31]

Grade 1	Predominant goblet cell component. Lack of aggressive features.
Grade 2	Predominant intermediate cell component. Aggressive invasion pattern but lacks other features of grade 3.
Grade 3	Predominant squamous cell component. Aggressive invasion pattern plus one or more of the following features: • necrosis • >4 mitoses per 10 high power fields • high-grade nuclear pleomorphism • perineural invasion • vascular invasion • bony invasion.

3.2 Acinic cell carcinoma

Acinic cell carcinomas are usually circumscribed but incompletely encapsulated. Cytologically low-grade tumours show several configurations (solid, papillary, follicular, clear-cell) but neither the configuration nor the cytological grade are generally accepted as useful indicators of behaviour,[10,34] and hence do not form part of a core dataset.

3.3 Adenoid cystic carcinoma

The histological type of adenoid cystic carcinoma is related to metastatic potential, with 0–4% of cribriform, hyaline and tubular carcinomas, and 33% of solid (basaloid) carcinomas metastasising to local lymph nodes.[9,35] Distant metastasis is more common in solid tumours.[10,30]

3.4 Carcinoma in pleomorphic adenoma

Carcinomas arising in pleomorphic adenomas may be of any histological type, but are thought to be particularly aggressive and the prognosis of the carcinomatous component is poorer than that of comparable carcinomas developing *de novo*.[9,10,36] Evidence for a pre-existing adenoma (remnants of myxochondroid stroma, focal scarring, hyalinised nodular 'ghost') should be sought in all carcinomas, particularly those showing multiple histological types and a varied histological appearance.

The extent of invasion should be measured for these tumours as it is prognostically useful, although precise criteria are not defined. Invasion more than 5–6 mm from the capsule of the residual adenoma is associated with a high risk of local recurrence and distant metastasis.[37,38]

Section C Neck dissection specimens

SPECIMEN REQUEST FORM

The type of neck dissection and node levels present should be specified by the surgeon using standard terminology.[39] It may be appropriate to use a request form that encourages the annotation of a schematic diagram to indicate the extent of the dissection. As the terminology applied to modified operations is potentially confusing, dissections should be described by specifying which node groups and non-lymphatic structures the surgeon has dissected and the relevant non-lymphatic structures that have been preserved or removed.

Three main types of neck dissection may be received:

- **comprehensive neck dissection**, which includes both radical and modified radical (functional) dissections. A radical neck dissection includes removal of cervical lymph nodes (levels I–V), sternomastoid muscle, internal jugular vein, spinal accessory nerve and the submandibular salivary gland, while in a functional dissection, the sternomastoid muscle, internal jugular vein, or the spinal accessory nerve may not be removed
- **selective neck dissection** involves removal of the nodal group(s) considered to be the most likely site for metastasis, preserving one or more nodal groups that are routinely removed in a radical dissection
- **extended neck dissection** when additional lymph node groups or non-lymphatic structures are removed.

Terminology of node groups

Six major anatomical groups (levels) of lymph nodes are described (see Figure 3).

- Level I: nodes of the submandibular and submental triangles.
- Levels II, III and IV: nodes of the upper, middle, and lower jugular chain. These nodes lie deep to the upper, middle and lower thirds of the sternocleidomastoid muscle respectively. The point at which the omohyoid muscle crosses deep to the sternocleidomastoid muscle is a useful landmark separating levels III and IV. Level IV extends from the omohyoid muscle to the clavicle.
- Level V: nodes of the posterior triangle, behind the posterior border of the sternocleidomastoid muscle.
- Level VI: nodes of the anterior compartment, around the midline visceral structures of the neck from the hyoid bone to the suprasternal notch.

Imaging studies may subclassify node levels II and V.[40] It is not suggested that this should be part of routine pathological practice but if separate groups are submitted, e.g. IIA and IIB, this should be noted in the pathology report.

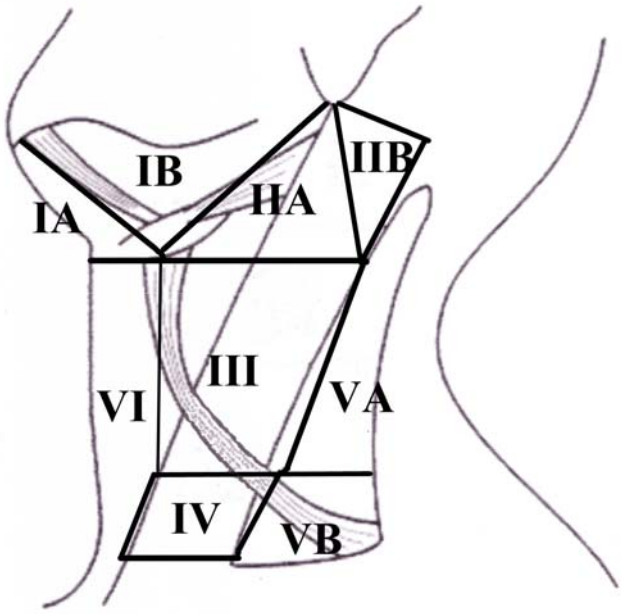

Figure 3 Diagrammatic representation of lymph node levels in the neck

PREPARATION OF THE SPECIMEN BEFORE DISSECTION

- Resection specimens should be orientated by the surgeon and pinned or sutured to cork or polystyrene blocks.
- The surgeon should indicate surgically critical margins and identify the general territories of node groups by placing markers such as metal tags or sutures at the centre of each anatomical group.
- A practical alternative for selective dissections is for the surgeon to separate the node groups, mark the superior margin of each group with a suture, and place each group in a separately labelled container.
- Nodes in addition to the main groups, e.g. parapharyngeal nodes, should be sent as separate specimens.
- Fixation is in a formaldehyde-based solution for 24–48 hours in a container of adequate size (the volume of fixative should be ten times that of the tissue).
- Photography of the specimen may be used to record the nature of the disease and the sites from which tissue blocks are selected. Surgically important margins may be marked with Indian ink or an appropriate dye.

NOTES ON DISSECTION AND BLOCK SELECTION

1. Identify the component structures. From the outer aspect: the submandibular salivary gland; the sternocleidomastoid muscle; the omohyoid muscle; the external jugular vein; the spinal accessory nerve; the tail of the parotid gland. Some dissections may include skin or other structures such as the stylohyoid and digastric muscles. From the deep aspect, identify the internal jugular vein.

2. Lymph nodes are identified by inspection and palpation around the vein, and around the submandibular gland and adipose tissue of the anterior and posterior triangles, and assigned to the appropriate anatomical level (this should be indicated by surgical markers). Each discrete node is dissected out with attached pericapsular adipose tissue. Larger nodes should be bisected or sliced. If there is obvious metastatic tumour, the half/slice with the more extensive tumour should be processed, together with the perinodal tissues to show the extent of extracapsular spread. If the node appears negative, all slices should be processed. Small or flat nodes should be processed whole, and several nodes (from the same anatomical level) can be processed in the same cassette. One H&E stained section from each block is usually sufficient for routine assessment.

3. An alternative method, that may be particularly useful for selective dissections is to serially slice the fixed specimen and to embed all of the tissue.[41] Care should be taken not to double-count larger nodes that are present in more than one block. Note that large nodes containing obvious metastatic carcinoma only need to be sampled to identify any extracapsular spread.

4. A radical neck dissection may yield an average of 20 nodes (range 10–30), in the absence of previous chemotherapy or irradiation, although on occasions 50–100 nodes may be identified. This examination would be expected to include, as a minimum, all palpable nodes greater than 3 mm in diameter.

5. Other blocks for histology: submandibular gland, jugular vein and sternomastoid if involved by tumour.

CORE DATA ITEMS TO BE INCLUDED IN THE HISTOPATHOLOGY REPORT

1 Clinical data (provided by the surgeon)

1.1 Nature of neck dissection (comprehensive or selective).

1.2 Node levels present.

2 Pathological data

2.1 At each anatomical level, record the total number of nodes identified and number of nodes involved by carcinoma. For practical purposes, the critical factor is involvement of levels IV or V. Including level III provides some leeway when describing spread so one is not forced into only saying upper or lower nodes are involved.

2.2 Size of largest metastatic deposit. Note that this is not the same as the size of the largest node. The size of the largest metastasis is a determinant in the TNM staging.[13]

2.3 Presence or absence of extra-capsular rupture and the node level(s) showing this feature. Extracapsular spread should be recorded as present or not identified. Any spread through the full thickness of the node capsule is recorded, and the previous separation into macroscopic and microscopic spread is now considered not to be necessary.[42] Involvement of adjacent anatomical structures should be recorded separately in the 'comments' section. If histological evidence of extracapsular spread is uncertain, it should be recorded as 'present'. This should prompt the use of adjuvant radiotherapy. Extracapsular spread is a manifestation of the aggressiveness of a carcinoma and is associated with a poor prognosis.[6,42–45]

2.4 The prognostic significance of micrometastases (<2 mm diameter) is not certain,[46,47] their presence should be included in the number of involved nodes and TNM coded as pN1(mi) or pN2(mi).

2.5 The 6th edition of the TNM classification[13] has introduced a category of pN0(i+) for nodes that contain clumps of isolated tumour cells (<0.2 mm) that are usually only detected by immunocytochemistry but may be seen on H&E stained sections. The prognostic significance of isolated tumour cells is not known for head and neck cancer, but studies of sentinel nodes may provide such data. At present, it is suggested that dissection and sectioning protocols are not modified, and that nodes containing isolated clumps of tumour cells are classified as pN0(i+) with the comment that "previously such cases would have been classified as pN+".

2.6 Involvement of lymphatic channels in neck is a poor prognostic factor, and may be mentioned in the text of the report.

2.7 If there is obvious metastatic disease with fusion (matting) of lymph nodes, record:

a) the level(s) of nodes involved by the mass
b) the maximum dimension
c) an estimate of the number of nodes that might be involved in the mass.

2.8 Isolated nodules of tumour in the connective tissue may represent discontinuous extensions of the primary tumour, soft tissue metastases or nodal metastases that have destroyed the node. Absolute distinction between these possibilities is not always possible and, while the 6th edition of the TNM classification[13] recommends regarding all deposits that do not have the contour of a node as discontinuous tumour extension, there does not appear to be any evidence for this approach in the head and neck. A practical approach is to regard any tumour nodule in the region of the lymphatic drainage as a nodal metastasis, and to only diagnose discontinuous extension of a carcinoma within 10 mm of the primary carcinoma and where there is no evidence of residual lymphoid tissue.

Other features form part of a complete description, but are not core data items

These features should be included as part of a comprehensive description of a neck dissection specimen but are of uncertain prognostic significance:

- presence of other pathology in cervical nodes
- presence of evidence of response of tumour, e.g. keratin debris, to previous therapy.

3 Diagnostic coding of metastases

pN status should be recorded according to the UICC guidelines[13] (see Appendix A), apart from the designation of isolated nodules of tumour cell (see Section 2.8).

4 Sentinel node biopsy

Sentinel lymph node biopsy has been suggested as a method to reduce the morbidity associated with cervical node dissections. This is currently an experimental technique for head and neck cancer patients and not part of standard patient care.[48,49] A standard dissection and sectioning protocol has yet to be defined, although current research studies use the following:[48]

- bisect or serially slice the node into 2.5 mm slices
- if node is negative on initial H&E sections, then:
  - step serial section at 150 μm intervals
  - one section from each level is stained with H&E
  - if these sections are negative, then immunocytochemical labelling with AE1/3 is performed; only morphologically viable labelled cells are counted as positive.

Cytological imprints and frozen section analysis are not part of the current research protocols.

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Appendix A TNM classification of malignant tumours[13]

GENERAL PRINCIPLES

PT Primary tumour

pTX Primary tumour cannot be assessed.

pT0 No evidence of primary tumour.

pTis Carcinoma *in situ.*

pT1, pT2, pT3, pT4: increasing size and/or local extent of the primary tumour (see specific sites).

pN Regional lymph nodes (for all primary sites, except nasopharynx)

pNX Nodes cannot be assessed.

pN0 No nodal metastasis.

pN0(i+) Isolated tumour cells only (<0.2 mm).

pN1(mi) Micrometastasis (2mm or less) only, in single node

pN1 Metastasis in single ipsilateral node 30 mm or less in diameter

pN2(mi) Micrometastasis (2 mm or less) only, in multiple or bilateral nodes

pN2a Metastasis in single ipsilateral node 31–60 mm diameter

pN2b Metastasis in multiple ipsilateral nodes <61 mm diameter

pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 60 mm in greatest dimension.

pN3 Metastasis in lymph node more than 60 mm diameter.

Notes

(i) For nasopharyngeal primary carcinomas:
pN1 – unilateral metastasis <61 mm above supraclavicular fossa
pN2 – bilateral metastases <61 mm above supraclavicular fossa
pN3 – metastasis in nodes >60 mm or in supraclavicular fossa.

(ii) Direct extension of a primary into a node is classified as nodal metastasis.

(iii) A tumour nodule >3 mm in the connective tissue without residual node is classified as a nodal metastasis. A nodule <3 mm is classified in pT as discontinuous extension.

(iv) When size is a criterion for pN classification, measure the size of the metastasis, and not that of the entire node.

(v) Midline nodes are considered ipsilateral.

M Distant metastasis

MX Distant metastasis cannot be assessed.

M0 No distant metastasis.

M1 Distant metastasis (may be subgrouped by site of metastasis).

SITE-SPECIFIC 'T' CODES

Lip, oral cavity and oropharynx

T1 Tumour 20 mm or less in greatest dimension.

T2 Tumour 21–40 mm in greatest dimension.

T3 Tumour >40 mm in greatest dimension.

T4 Tumour invades adjacent structures.

Nasopharynx

T1 Tumour confined to nasopharynx.

T2 Tumour extends to soft tissue of oropharynx and/or nasal fossa.

T3 Tumour invades bone and/or paranasal sinuses.

T4 Tumour with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx or orbit.

Hypopharynx

T1 Tumour limited to one subsite and 20 mm or less in greatest dimension.

T2 Tumour involves more than one subsite or measures 21–40 mm in size.

T3 Tumour >40 mm in size or with fixation of hemilarynx.

T4 Tumour invades adjacent structures.

Larynx, supraglottis

T1 Tumour limited to one subsite with normal vocal cord mobility.

T2 Tumour invades more than one adjacent subsite without fixation of larynx.

T3 Tumour limited to larynx with vocal cord fixation, and/or invades postcricoid area, pre-epiglottic tissues or deep base of tongue.

T4 Tumour invades through thyroid or cricoid cartilage and/or invades tissues beyond the larynx, e.g. soft tissues of neck, thyroid or into oesophagus.

Larynx, glottis

T1 Tumour limited to vocal cords with normal mobility.

T2 Tumour extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility.

T3 Tumour limited to larynx with vocal cord fixation and/or invades the paraglottic space and/or with invasion of inner cortex of thyroid cartilage.

T4 Tumour invades through thyroid or cricoid cartilage and/or invades tissues beyond the larynx, e.g. soft tissues of neck, thyroid or into oesophagus.

Larynx, subglottis

T1 Tumour limited to subglottis.

T2 Tumour extends to vocal cords with normal or impaired mobility.

T3 Tumour limited to larynx with vocal cord fixation.

T4 Tumour invades through thyroid or cricoid cartilage and/or invades tissues beyond the larynx, e.g. soft tissues of neck, thyroid or into oesophagus.

Maxillary sinus

T1 Tumour limited to antral mucosa with no bone involvement.

T2 Tumour causing bone erosion or destruction, except for posterior wall.

T3 Tumour invades posterior wall of sinus, subcutaneous tissues, floor or medial wall of orbit, infratemporal fossa, pterygoid plate, ethmoid sinuses.

T4 Tumour invades skin of cheek, orbital contents beyond floor and medial wall, base of skull, nasopharynx, sphenoid sinus or frontal sinus.

Nasal cavity and ethmoid sinus

T1 Tumour restricted to one subsite in the nasal cavity or ethmoid sinus, with or without bone erosion.

T2 Tumour involves two subsites** within one site or extends to involve an adjacent site within the. nasoethmoidal complex, with or without bone erosion.

T3 Tumour extends to involve the medial wall or floor of the orbit, maxillary sinus, palate or cribriform plate.

T4 Tumour with intracranial extension, anterior orbital extension, or involves sphenoid or frontal sinuses and/or skin of nose.

** Sites for classification are the individual maxillary and ethmoidal sinuses and the nasal cavity. The nasal cavity is divided in the following subsites: septum, floor, lateral floor and vestibule.

Major salivary glands

Tx Primary tumour cannot be assessed.

T0 No evidence of primary tumour.

T1 Tumour 20 mm or less in greatest dimension without extraparenchymal extension.

T2 Tumour more than 20 mm but not more than 40 mm in greatest dimension without extraparenchymal extension.

T3 Tumour more than 40 mm and/or tumour with extraparenchymal extension.

T4a Tumour invades skin, mandible, ear canal or facial nerve.

T4b Tumour invades base of skull, pterygoid plates or encases carotid artery.

Note: Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve except those listed under T4a or b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

Appendix B SNOMED 'T' codes

SNOMED 'T' code	Sites and subsites
T-52000	**Lip**
T-52230	External upper lip (vermilion border)
T-52240	External lower lip (vermilion border)
T-52003	Commisures
T-51000	**Oral cavity**
T-51300	Buccal mucosa
T-52250	Mucosa of upper and lower lips
T-51030	Cheek mucosa
T-51600	Retromolar areas
T-51010	Bucco-alveolar sulci
T-54920	Upper alveolus and gingiva (upper gum)
T-54930	Lower alveolus and gingiva (lower gum)
T-51110	Hard palate
T-53000	**Tongue**
T-53120	Dorsum and lateral borders of anterior 2/3
T-53123	Inferior (ventral) surface
T-51200	Floor of mouth
T-60200	**Oropharynx**
T-53122	Anterior wall (glosso-epiglottic area)
T-53130	Base of tongue
T-60230	Vallecula
T-60220	Lateral wall
T-61100	Tonsil
T-61240	Tonsillar fossa and pillars
T-61150	Tonsillar pillars
T-60210	Posterior wall
	Superior wall
T-51120	Inferior surface of soft palate
T-51130	Uvula
T-23000	**Nasopharynx**
T-23001	Postero-superior wall
T-23002	Lateral wall (includes fossa of Rosenmuller)
T-51122	Inferior wall (superior surface of soft palate)

SNOMED 'T' code	Sites and subsites
T-60300	**Hypopharynx**
T-24080	Pharyngo-oesophageal junction (post-cricoid area)
T-60320	Piriform sinus
T-60350	Posterior pharyngeal wall
T-24100	**Larynx**
T-24010	Epiglottis
T-24310	Aryepiglottic fold, laryngeal aspect
T-24320	Ventricular bands (false cords)
T-24440	Glottis
T-24400	Vocal cords
T-24470	Commissures
T-24450	Subglottis
T-21000	**Nose**
T-21030	Olfactory region of nose
T-21320	Nasal vestibule
T-21340	Nasal septum
T-21360	Nasal turbinate
T-22000	**Paranasal sinuses**
T-22100	Maxillary sinus
T-22200	Frontal sinus
T-22300	Ethmoid sinus
T-22400	Sphenoid sinus
T-55000	**Salivary glands**
T-55100	Parotid gland
T-55200	Submandibular gland
T-55300	Sublingual gland
T-55400	Minor salivary gland

Appendix C SNOMED 'M' codes

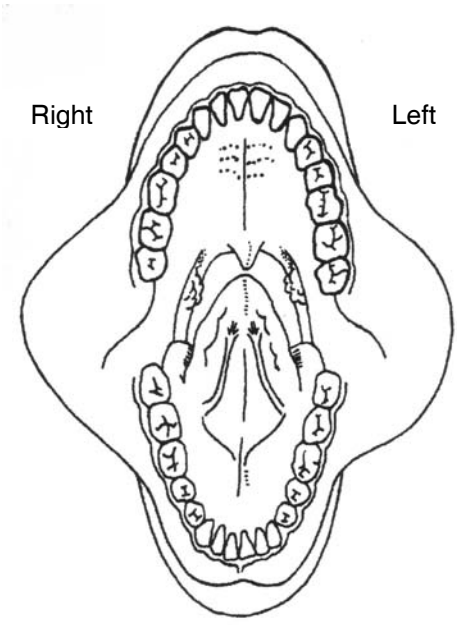
Note: This is not a comprehensive list of all malignancies and other codes should be used as necessary.

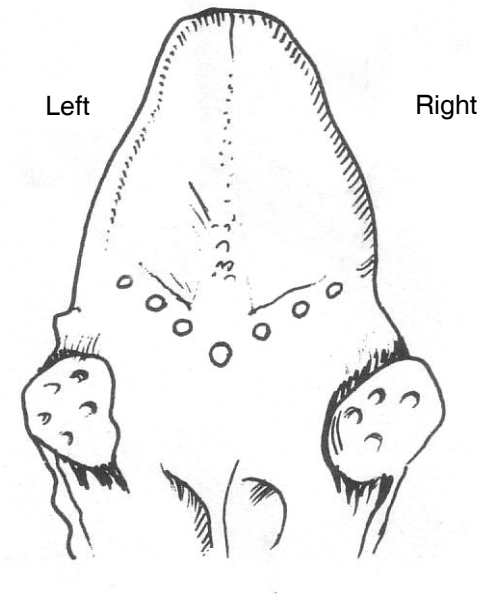
	Squamous carcinoma and variants
M-80702	Squamous carcinoma in situ
M-80703	Squamous carcinoma
M-80705	Microinvasive squamous carcinoma
M-80713	Keratinising squamous carcinoma
M-80723	Non-keratinising squamous carcinoma
M-80743	Spindle cell squamous carcinoma
M-80753	Adenoid squamous carcinoma
M-85603	Adenosquamous carcinoma
	Salivary malignancies
M-85503	Acinic cell carcinoma
M-84303	Mucoepidermoid carcinoma
M-82003	Adenoid cystic carcinoma
M-82003	Polymorphous low grade adenocarcinoma (terminal duct adenocarcinoma)
M-85623	Epithelial-myoepithelial carcinoma
M-81473	Basal cell adenocarcinoma
M-84103	Sebaceous carcinoma
M-84503	Papillary cystadenocarcinoma
M-84803	Mucinous adenocarcinoma
M-82903	Oncocytic carcinoma
M-85003	Salivary duct carcinoma
M-81403	Adenocarcinoma
M-89823	Malignant myoepithelioma (myoepithelial carcinoma)
M-89413	Carcinoma in pleomorphic adenoma (malignant mixed tumour)
M-80703	Squamous cell carcinoma
M-80413	Small cell carcinoma
M-80203	Undifferentiated carcinoma

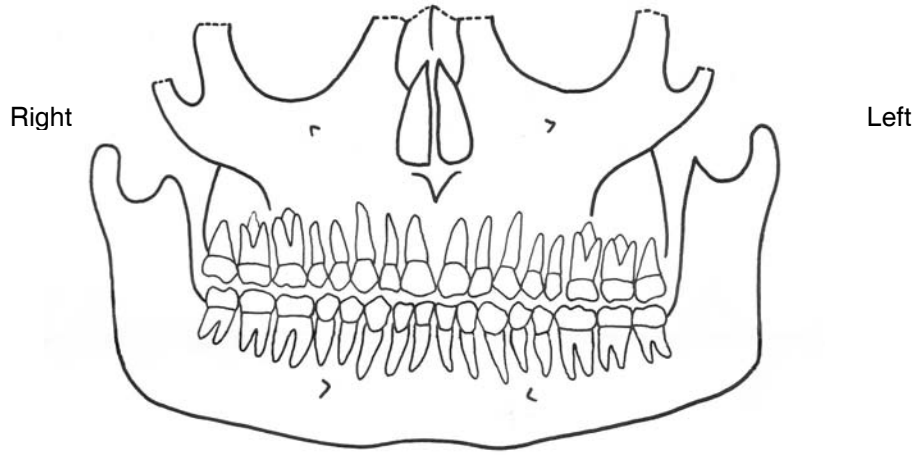
Appendix D Draft request forms for primary mucosal carcinomas and node dissections

Surname:	Consultant:
Forename:	Location:
Date of birth:	
Sex:	
Hospital number:	NHS no.:

Relevant medical or dental history:	**Clinical diagnosis:**
Site of lesion:	Previous reports (laboratory number, if known):
Duration of symptoms:	
Predisposing factors:	Other information:
Date of operation:	
Signature:	



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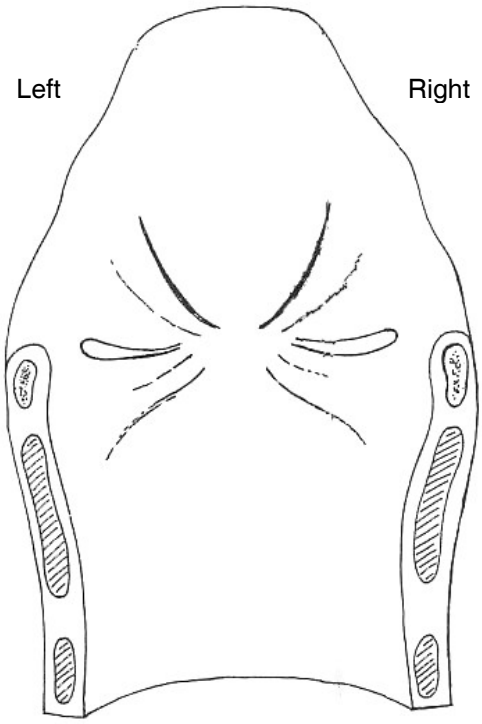
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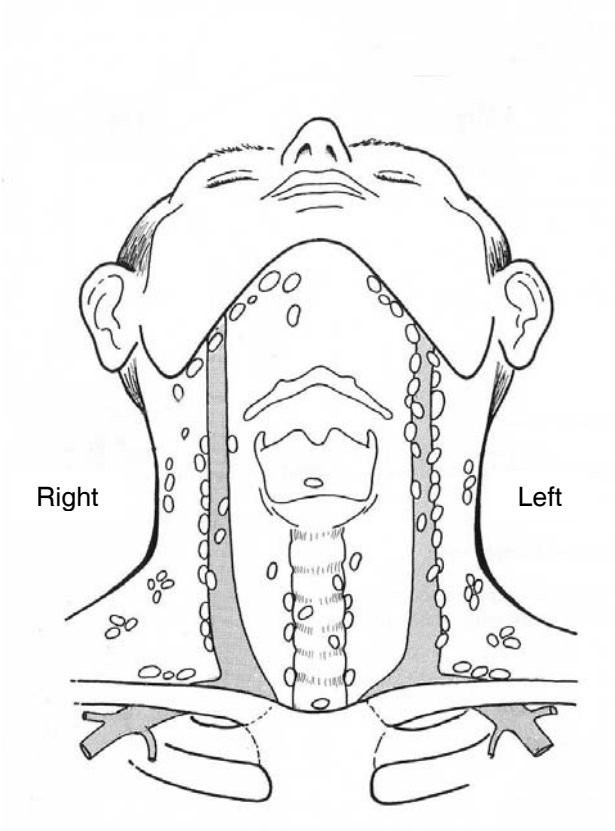
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Appendix E Reporting proformas

HEAD AND NECK CARCINOMA DATASET

Surname ……..….. Forenames ……..….. Date of birth …...… … Sex ….....

Hospital …… Hospital no ……... NHS no …...……..…….……

Date of receipt …….…… Date of report ……..…. Report no ……..…….…….…….....

Pathologist ……..…….. Surgeon ……...…….…...……..……..…

Clinical TNM stage …… Previous radiotherapy Yes □ No □ Unknown □

T…… N…… M…… Previous chemotherapy Yes □ No □ Unknown □

Primary tumour

Site …….

Subsite(s) …….…..

Right □ Left □ Midline □

Type of resection ……..

Histological type: Squamous carcinoma □

Other/subtype……..

Differentiation Well □

Moderate □

Poor □

Invasive front Cohesive□ Non-cohesive □

Maximum diameter ……. (mm)

Maximum depth of invasion …….. (mm)

Distance from invasive tumour to

mucosal margin …….……. (mm)

deep margin ……...……..… (mm)

Vascular invasion	Yes □	No □
Nerve invasion	Yes □	No □
Bone/cartilage invasion	Yes □	No □
Severe dysplasia present	Yes □	No □
Severe dysplasia at margin	Yes □	No □

Right neck dissection: Yes □ No □

Comprehensive □ Selective □

Node levels present: I II III IV V VI Other □

Total number of nodes……

Number positive nodes……...

Levels with metastases: I II III IV V VI Other □

Largest metastasis …..…….. (mm)

Extracapsular spread Yes □ No □

Levels with ECS……

Left neck dissection: Yes □ No □

Comprehensive □ Selective □

Node levels present: I II III IV V VI Other □

Total number of nodes……

Number positive nodes……...

Levels with metastases: I II III IV V VI Other □

Largest metastasis …..…….. (mm)

Extracapsular spread Yes □ No □

Levels with ECS……

Summary of pathological data:

Tumour site…….……

New primary □ Recurrence □ Not known □

Tumour type……

pTNM stage pT….. pN…….pM…...…

SNOMED codes

T……M…….

T……M…….

Resection of primary tumour clear □ close □ involved □

Signed: **Date:**

SALIVARY CARCINOMA DATASET

Surname ……..….. Forenames ……..….. Date of birth ……...…... Sex ….....

Hospital …… Hospital no ……... NHS no …...…….…….……

Date of receipt ……..…… Date of report ……..…. Report no ……..…….…….…....

Pathologist ……..…….. Surgeon ……...…...…...……..……..…

Primary tumour

Site: Parotid □ Submandibular □ Sublingual □ Left / Right

Other □ Please specify ……..……

Histological type ……..

Histological grade (if appropriate) ……

Maximum dimension …… (mm)

Macroscopic extraglandular extension: Yes / No

Minimum excision margin ……...… (mm)

Right neck dissection: Yes □ No □

Comprehensive □ Selective □

Node levels present: I II III IV V VI Other □

Total number of nodes……

Number positive nodes……...

Levels with metastases: I II III IV V VI Other □

Largest metastasis …..…….. (mm)

Extracapsular spread Yes □ No □

Levels with ECS……

Left neck dissection: Yes □ No □

Comprehensive □ Selective □

Node levels present: I II III IV V VI Other □

Total number of nodes……

Number positive nodes……...

Levels with metastases: I II III IV V VI Other □

Largest metastasis …..…….. (mm)

Extracapsular spread Yes □ No □

Levels with ECS……

Comments/additional information:

Summary of pathological data:

pTNM stage pT….. pN…….pM…..…

Tumour site……..……

SNOMED codes

New primary □ Recurrence □ Not known □

T……M…….

Tumour type……

T……M…….

Resection of primary tumour clear □ close □ involved □

Signed: **Date:**