



Carcinomas of the Hypopharynx, Larynx and Trachea Histopathology Reporting Guide

Family/Last name Date of birth Given name(s) Patient identifiers Date of request Accession/Laboratory number Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.[SCOPE OF THIS DATASET](#)**NEOADJUVANT THERAPY** (Note 1)

- Information not provided
 Not administered
 Administered, *specify type*

- Chemotherapy
 Radiotherapy
 Targeted therapy, *specify if available*

- Immunotherapy, *specify if available*

OPERATIVE PROCEDURE (select all that apply) (Note 2)

- Not specified
 Biopsy (excisional, incisional), *specify*

- Resection, *specify*

- Neck (lymph node) dissection*, *specify*

- Other, *specify*

* If a **neck dissection** is submitted, then a separate dataset is used to record the information.

SPECIMENS SUBMITTED (select all that apply) (Note 3)

- Not specified
 Trachea
 Hypopharynx
 Laryngopharyngectomy
 Other, *specify*

 Larynx

- Endolaryngeal excision
 Transoral laser excision
 Supraglottic laryngectomy
 Supracricoid laryngectomy
 Total laryngectomy
 Vertical hemilaryngectomy, *specify side*

- Partial laryngectomy, *specify type*

- Other, *specify*

SPECIMEN DIMENSIONS (Note 4)

Maximum dimension

 mm

Additional dimensions

 mm x mm
TUMOUR SITE (select all that apply) (Note 5)

- Cannot be assessed
 No macroscopically visible tumour
 Trachea
 Left Right
 Midline Laterality not specified

 Hypopharynx

- Left Right
 Midline Laterality not specified

- Piriform sinus
 Postcricoid
 Pharyngeal wall (posterior and/or lateral)
 Other, *specify*

- Larynx, supraglottis
- Left Right
- Midline Laterality not specified
- Epiglottis
- Lingual aspect
- Laryngeal aspect
- Aryepiglottic fold
- Arytenoid
- False vocal cord/fold
- Ventricle

- Larynx, glottis
- Left Right
- Midline Laterality not specified
- True vocal cord/fold
- Anterior commissure
- Posterior commissure

- Larynx, subglottis
- Left Right
- Midline Laterality not specified

Other, *specify including laterality*

TUMOUR FOCALITY

- Unifocal
- Multifocal, *specify number of tumours in specimen*
-
- Cannot be assessed, *specify*
-

TUMOUR DIMENSIONS (Note 6)

Maximum tumour dimension (largest tumour)

mm

Additional dimensions (largest tumour)

mm x mm

Cannot be assessed, *specify*

HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 7)
 (Value list from the World Health Organization Classification of Head and Neck Tumours (2017))

- Squamous cell carcinoma, conventional type
- Squamous cell carcinoma, variant types
- Adenosquamous carcinoma
- Basaloid squamous cell carcinoma
- Papillary squamous cell carcinoma
- Spindle cell squamous cell carcinoma
- Verrucous squamous cell carcinoma
- Lymphoepithelial carcinoma
- Neuroendocrine carcinoma
- Well differentiated neuroendocrine carcinoma
- Moderately differentiated neuroendocrine carcinoma
- Poorly differentiated neuroendocrine carcinoma
- Small cell neuroendocrine carcinoma
- Large cell neuroendocrine carcinoma
- Combined (or composite) neuroendocrine carcinoma, with squamous or adenosquamous component
- Carcinomas of Minor Salivary Glands
- Adenoid cystic carcinoma, *specify grade*
-
- Mucoepidermoid carcinoma, *specify grade*
-
- Other, *specify*
-
- Other, *specify*
-

HISTOLOGICAL TUMOUR GRADE (Note 8)

- Not applicable
- GX: Cannot be assessed
- G1: Well differentiated
- G2: Moderately differentiated
- G3: Poorly differentiated
- Other, *specify*
-

EXTENT OF INVASION (select all that apply) (Note 9)

- Larynx**
- Not identified
- Involves mucosa
- Involves paraglottic space
- Involves pre-epiglottic space
- Partial thickness invasion of cartilage
- Full thickness invasion of cartilage

Tumour thickness

mm

Hypopharynx

Tissue layers involved, *specify*

Tumour thickness

mm

PATTERN OF INVASIVE FRONT (Note 10)

(Resection specimens only, not applicable to biopsies)

- Cohesive
- Non-cohesive

PERINEURAL INVASION (Note 11)

- Not identified
- Present
- Cannot be assessed, *specify*

▼

LYMPHOVASCULAR INVASION (Note 12)

- Not identified
- Present
- Cannot be assessed, *specify*

▼

MARGIN STATUS (Note 13)

Invasive carcinoma

- Involved

▼ Specify margin(s), if possible

- Not involved

Distance from closest margin mm

- Distance not assessable

Specify closest margin, if possible

Carcinoma in situ/high-grade dysplasia**

- Involved

▼ Specify margin(s), if possible

- Not involved

Distance from closest margin mm

- Distance not assessable

Specify closest margin, if possible

- Cannot be assessed, *specify*

▼

** High-grade dysplasia is synonymous with moderate/severe dysplasia.

COEXISTENT PATHOLOGY (select all that apply) (Note 14)

- None identified
- Necrotizing sialometaplasia
- Infection, *specify*

▼

- Dysplasia, *specify type and grade*

▼

- Hyperplasia, *specify*

▼

- Other, *specify*

▼

ANCILLARY STUDIES (Note 15)

- Not performed
- Performed, *specify*

▼

PATHOLOGICAL STAGING (UICC TNM 8th edition) (Note 16)**

TNM Descriptors (only if applicable) (select all that apply)

- m - multiple primary tumours
- r - recurrent
- y - post-therapy

Primary tumour (pT)***

- TX Primary tumour cannot be assessed
- Tis Carcinoma in situ

Primary tumour: Hypopharynx

- T1 Tumour limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension
- T2 Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest dimension without fixation of hemilarynx
- T3 Tumour more than 4 cm in greatest dimension, or with fixation of hemilarynx or extension to oesophageal mucosa
- T4a Moderately advanced local disease
Tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus, or central compartment soft tissue#
- T4b Very advanced local disease
Tumour invades prevertebral fascia, encases carotid artery, or invades mediastinal structures

*** Note that the results of lymph node/neck dissection are derived from a separate dataset.

Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

Primary tumour: Supraglottis

- T1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility
- T2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g. mucosa of base of tongue, vallecula, medial wall of piriform sinus) without fixation of the larynx
- T3 Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage
- T4a Moderately advanced local disease
Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, or oesophagus
- T4b Very advanced local disease
Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

Primary tumour: Glottis

- T1 Tumour limited to the vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
- T1a Tumour limited to one vocal cord
- T1b Tumour involves both vocal cords
- T2 Tumour extends to supraglottis and/or subglottis and/or with impaired vocal cord mobility
- T3 Tumour limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or inner cortex of the thyroid cartilage
- T4a Tumour invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscle of the tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus
- T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

Primary tumour: Subglottis

- T1 Tumour limited to subglottis
- T2 Tumour extends to vocal cord(s) with normal or impaired mobility
- T3 Tumour limited to larynx with vocal cord fixation
- T4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx e.g. trachea, soft tissues of neck including deep/extrinsic muscles of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus
- T4b Tumour invades prevertebral space, encases carotid artery, or mediastinal structures

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Scope

The dataset has been developed for the reporting of resection and biopsy specimens of mucosal malignancies of the larynx, hypopharynx and trachea. The protocol applies to all invasive carcinomas of the larynx, hypopharynx and trachea (including the supraglottis, glottis, and subglottis). Salivary-type malignancies arising from mucosal glands of the hypopharynx and larynx should be recorded in this dataset; the paucity of prognostic or predictive data suggest that tumour type and grade (as described in the International Collaboration on Cancer Reporting (ICCR) *Carcinomas of the major salivary glands dataset*¹), size and margin status should be recorded. Mucosal melanoma is presented in a separate dataset. Lymphomas and sarcomas are not included. Malignancies arising at other sites in the head and neck region, and neck dissections and nodal excisions are dealt with in separate datasets which may be used, as appropriate, in conjunction with this dataset.

Where more than one anatomically or histologically distinct primary tumours occur, a separate dataset should be completed for each tumour.

TRACHEAL CARCINOMAS

Tracheal malignancies are rare and represented in the literature as single case reports and small series of cases. Most reports describe squamous cell carcinomas and carcinomas arising from the salivary glands.²⁻⁶ Too few cases are reported to analyse prognostic or predictive data and there is no TNM classification for tracheal malignancies under either the Union for International Cancer Control (UICC) or American Joint Committee on Cancer (AJCC) systems.

Pragmatically, this dataset suggests that the data from squamous cell carcinomas are recorded using the hypopharyngeal carcinoma dataset as a template. In particular, tumour size (maximum diameter) and depth of invasion should be recorded.

Note 1 – Neoadjuvant therapy (Non-core)

Reason/Evidentiary Support

Information from the surgeon about the use of neoadjuvant therapy will help the pathologist interpret correctly the histologic findings. While the extent of tumour necrosis or post-therapy fibrosis are not currently used as an important guide to management for most types of laryngeal cancer, it is good practice to document the effects of previous treatment as part of a free text report. Pragmatically, an estimate of the amount (% tumour volume) of necrosis or fibrosis can be provided as free text.

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Note 2 – Operative procedure (Core)

Reason/Evidentiary Support

The nature of the operative procedure will influence the required level of detail in the pathological report. Diagnostic/incisional biopsies will usually generate a limited set of data items compared to excision/resection specimens and, for example, the status of resection margins does not require detailed consideration for diagnostic biopsies except for very small carcinomas where the entire cancer may be present in the diagnostic specimen.

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Note 3 – Specimens submitted (Core)

Reason/Evidentiary Support^{7,8}

The pathologist needs to be informed about the nature of surgery (type of specimen) so that their description and dissection are focused on selecting appropriate tissues to guide accurate cancer staging.

The following commentary is intended to assist pathologists to understand the complex anatomy of the larynx and related structures. Anatomical sites and tissue compartments of the larynx are shown in Figures 1 and 2.

The **supraglottis** includes the epiglottis, aryepiglottic fold (laryngeal aspect), arytenoid, ventricular bands (false cords) and laryngeal ventricles.

The **glottis** extends from the ventricle to approximately 1.0 cm below the free level of the true vocal cord and includes the vocal cords, anterior commissure and posterior commissure.

The **subglottis** extends from approximately 1.0 cm below the level of the true vocal cord to the inferior rim of the cricoid cartilage.

Note that transglottic carcinomas cross the ventricles in a vertical direction arising in either the glottic and/or supraglottic larynx.

The **hypopharynx** is the part of the pharynx extending from the plane of the superior border of the hyoid bone (or floor of the vallecula) to the plane corresponding to the lower border of the cricoid cartilage. The contents of the hypopharynx include:

- left and right piriform sinuses which expand bilaterally and forward around the sides of the larynx and lie between the larynx and the thyroid cartilage
- lateral and posterior hypopharyngeal walls
- postcricoid region extending from the level of the arytenoid cartilages to the inferior border of the cricoid cartilage.

The **paraglottic space** is a potential space antero-lateral and deep to the ventricles and saccules, and filled with adipose tissue and connective tissue (Figure 1). It is bounded by the conus elasticus

inferiorly, the thyroid cartilage laterally, the quadrangular membrane medially, and the piriform sinus posteriorly.

The **pre-epiglottic space** is anterior to the base of the epiglottis and filled with adipose tissue and connective tissue (Figure 2); it is triangular in shape and is bounded by the thyroid cartilage and thyrohyoid membrane anteriorly, the epiglottis and thyroepiglottic ligament posteriorly, and the hyoepiglottic ligament at its base (Figures 1 and 2).

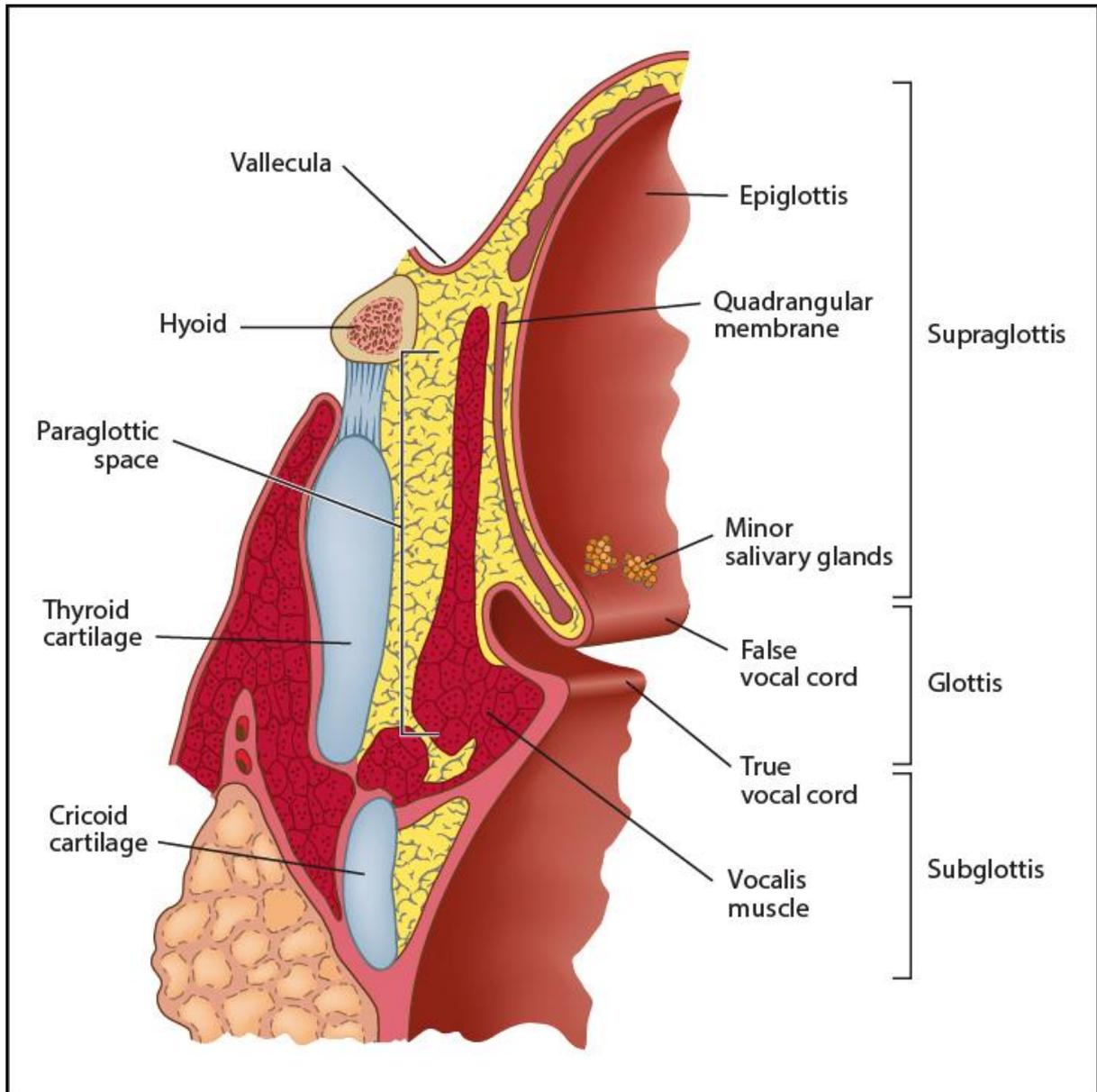


Figure 1. Coronal section through the larynx to show the main structures and paraglottic space

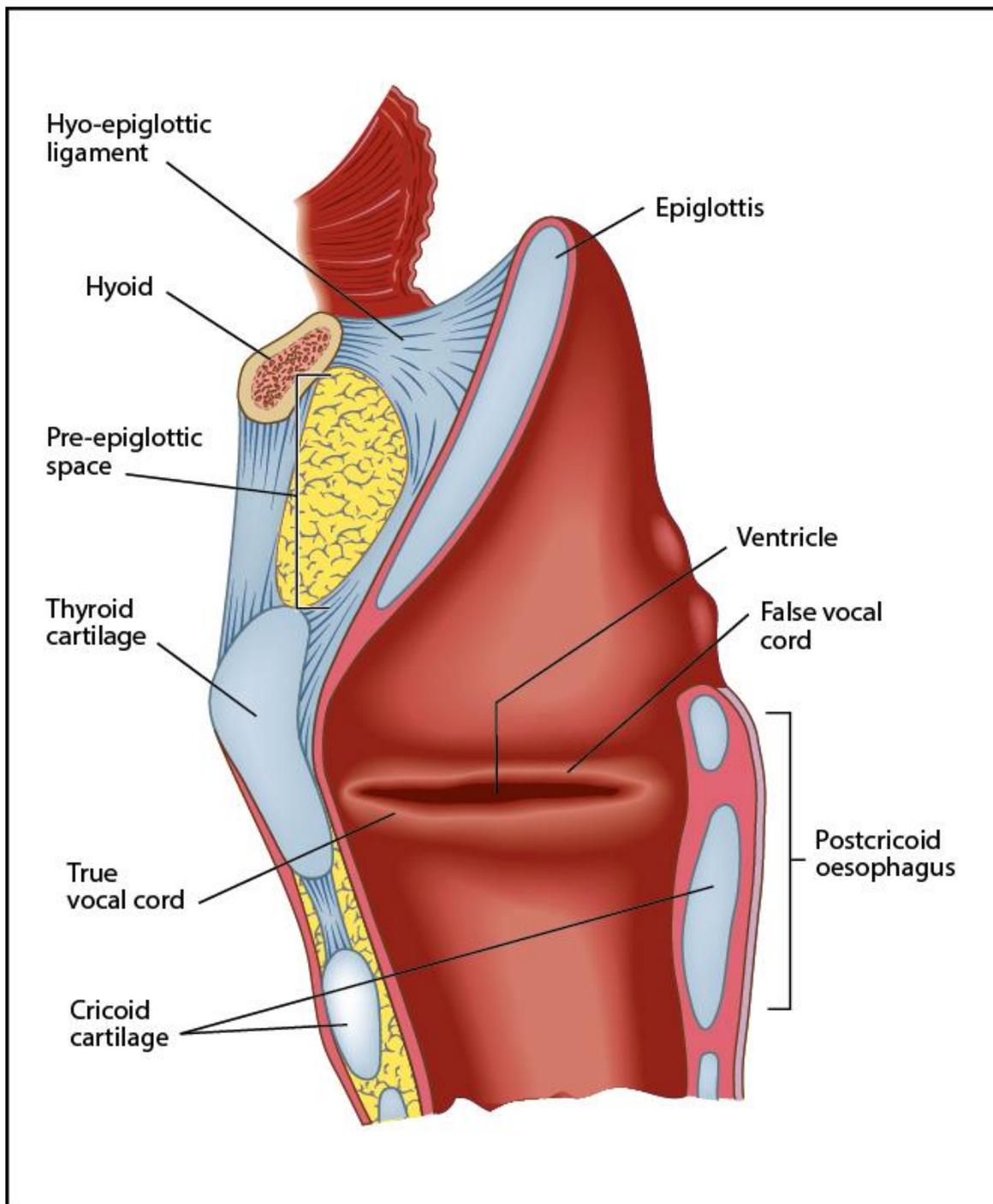


Figure 2. Sagittal section through the larynx to show main structures and the pre-epiglottic space

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Note 4 – Specimen dimensions (Core and non-core)

Reason/Evidentiary Support

The size of a resection specimen is useful as it places the size of the tumour into the operative context. In those rare instances where specimens may be mislabelled, the size of the tissue may help to resolve any discrepancies.

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Note 5 – Tumour site (Core)

Reason/Evidentiary Support⁹

Accurate documentation of the laterality and site of the specimen and tumour avoids errors in the delivery of therapy. The site of the primary tumour is a key determinant in clinicopathological staging systems for hypopharynx and larynx.

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 UICC nomenclature.¹⁰

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Note 6 – Tumour dimensions (Core and Non-core)

Reason/Evidentiary Support^{10,11}

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

For larynx, several sites rely on the presence or absence of vocal cord mobility to determine T stage; in these circumstances, only a provisional pT stage can be offered (at least pT1a, for example).

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Note 7 – Histological tumour type (Core)

Reason/Evidentiary Support^{9,12-14}

Histopathological type is important for cancer registration and prognosis, with strength of evidence varying for different types. Verrucous and papillary carcinomas tend to have a good prognosis while, adenosquamous carcinomas have a worse prognosis than conventional and spindle cell carcinomas. For most of the variants of squamous cell carcinoma, surgery with adequate margins is the main treatment. In some tumours, such as large cell neuroendocrine carcinomas, a combination of irradiation and chemotherapy is indicated.

All tumours of the hypopharynx, larynx and trachea should be given a type based on the most recent edition of the World Health Organization (WHO) Classification of Head and Neck Tumours.⁹

WHO classification of tumours of the hypopharynx, larynx and trachea^{a9}

Descriptor	ICD-O codes
Malignant surface epithelial tumours	
Conventional squamous cell carcinoma	8070/3
Verrucous squamous cell carcinoma	8051/3
Basaloid squamous cell carcinoma	8083/3
Papillary squamous cell carcinoma	8052/3
Spindle cell squamous carcinoma	8074/3
Adenosquamous carcinoma	8560/3
Lymphoepithelial carcinoma	8082/3
Neuroendocrine tumours	
Well-differentiated neuroendocrine carcinoma	8240/3
Moderately differentiated neuroendocrine carcinoma	8249/3
Poorly differentiated neuroendocrine carcinoma	
Small cell neuroendocrine carcinoma	8041/3
Large cell neuroendocrine carcinoma	8013/3

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.

For salivary-type tumour arising from mucosal glands, please refer to the *ICCR Carcinomas of the major salivary glands* dataset¹ for descriptors and ICD-O codes.

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Note 8 – Histological tumour grade (Core)

Reason/Evidentiary Support^{9,15-20}

Although human papillomavirus (HPV)-associated carcinomas arising in the oropharynx are graded differently from conventional (non-HPV) carcinomas (see ICCR *Carcinomas of the nasopharynx and oropharynx* dataset²¹), there is insufficient evidence to justify this approach in the hypopharynx and larynx. The recommendation is that HPV assessment should not be performed except for basaloid carcinomas. The conventional grading system for classical squamous cell carcinomas should be used for all tumours at these sites.

Grading is based on the degree of resemblance of the carcinoma to the normal epithelium and follows the descriptions in the WHO classification. The most aggressive area is graded as well, moderately or poorly differentiated. This system is widely used and prognostically useful, even though it suffers from inter-observer variability and sampling problems. While most squamous cell carcinomas will be well differentiated, it is important for prognostication to separate tumours based on differentiation. Where a tumour has a varied appearance, then the highest grade (poorest differentiation) is recorded as a core data item, while the predominant pattern may be recorded as non-core data.

Squamous cell carcinoma variants (basaloid, adenosquamous, spindle cell) are considered to have intrinsic biological potential and are not graded.

For the grading of salivary-type tumour arising from mucosal glands, please refer to the ICCR *Carcinomas of the major salivary glands* dataset¹ for descriptors.

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Note 9 – Extent of invasion (Core and Non-core)

Reason/Evidentiary Support^{7,10,11,22}

In the larynx, the invasion of tissue compartments deep to the mucosa is important for staging. The important tissues for staging purposes are the paraglottic space, the pre-epiglottic space and the thyroid and cricoid cartilages. One of the points of distinction between T3 and T4a carcinomas is whether cartilage invasion is minor (partial) or full thickness. The absolute tumour thickness is non-core for larynx and hypopharynx.

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Note 10 – Pattern of invasive front (Non-core)

Reason/Evidentiary Support^{15,23}

The pattern of invasion by the carcinoma at its deep margin is of proven prognostic value for oral and oropharyngeal carcinomas and there is limited evidence that a similar approach may be of value

to predict nodal metastasis for hypopharyngeal and laryngeal carcinomas. Note that the response for this data item is based on the most complex ('worst') area of the carcinoma. The pattern of invasion is included as a non-core data item as many head and neck pathologists include this in their personal descriptive assessment of carcinomas at all sites, and it is convenient to use it for larynx and pharynx as well, for consistency with national dataset, even though this is not supported by robust evidence of clinical impact.

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Note 11 – Perineural invasion (Core)

Reason/Evidentiary Support^{20,23-28}

The presence or absence of perineural invasion should be recorded, regardless of the size of the nerve. Invasion of the perineural plane is a predictor of local recurrence and nodal metastasis and may prompt consideration of adjuvant chemoradiotherapy.

The perineural plane is a potential space between the bundles of axons and the perineurium; the presence of carcinoma around a nerve (external to the perineurium) is not regarded as perineural invasion. There is some evidence that extratumoural perineural invasion is of more importance than intratumoural perineural invasion but this requires confirmation. For this dataset, either intratumoural or extratumoural invasion is regarded as a positive finding.

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Note 12 – Lymphovascular invasion (Core)

Reason/Evidentiary Support^{29,30}

Lymphovascular invasion is a relatively weak predictor of nodal metastasis.

The presence of carcinoma cells within an endothelial-lined space is the essential criterion and should be distinguished from retraction artefact. It is not necessary to distinguish between small lymphatics and venous channels.

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Note 13 – Margin status (Core)

Reason/Evidentiary Support³¹⁻⁴²

Margin status is a predictor of local recurrence and may require consideration of adjuvant therapy. The status of the surgical resection margin should include assessment of both invasive and in situ carcinoma.

A positive margin is one in which the carcinoma is present at the margin while the definition of a ‘close margin’ varies between published series, typically being regarded as between 3 and 5 mm. For laser resections of glottic carcinomas even 1 mm may be adequate due to the thermal damage of tissue at the margin. It is recommended that the distance from in situ or invasive carcinoma to the closest margin is recorded, if assessable. Note that comment on the deep resection margin of a laryngectomy specimen may be inapplicable unless the tumour extends close to the base of tongue or into the soft tissues of the neck.

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Note 14 – Coexistent pathology (Non-core)

This is a non-core data item to provide the pathologist with the flexibility to record any other diseases that potential impact on clinical management, such as infections.

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Note 15 – Ancillary studies (Non-core)

Reason/Evidentiary Support

This is a non-core data item that is intended to allow pathologists to record the use of additional investigations, particular molecular testing, the prognostic and predictive significance of which is uncertain.

The literature recognises that a very few HPV associated carcinomas may occur in the hypopharynx and larynx, but prognostic relevance is uncertain.⁴³

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Note 16 – Pathological staging (Core)

Reason/Evidentiary Support

By AJCC/UICC convention, the designation “T” refers to a primary tumour that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection

of the primary tumour or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumour. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumour has been completely removed. If a biopsied tumour is not resected for any reason (e.g. when technically unfeasible) and if the highest T and N categories or the M1 category of the tumour can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

UICC TNM 8¹⁰

Primary Tumour: Subglottis

Note that the UICC and AJCC staging differs for T3/T4a subglottic carcinomas. In the AJCC system, T3 carcinomas include those limited to larynx with vocal cord fixation and/or invasion of paraglottic space and/or inner cortex of the thyroid cartilage.

Larynx:

Normal (T1) or impaired (T2) vocal cord mobility and vocal cord fixation (T3) may only be determined clinically.

TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y” and “r” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumours in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e. neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumour actually present at the time of that examination. The “y” categorization is not an estimate of tumour prior to multimodality therapy (i.e. before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumour when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

Additional Descriptors

Residual Tumour (R)

Tumour remaining in a patient after therapy with curative intent (e.g. surgical resection for cure) is categorized by a system known as R classification, shown below.

RX Presence of residual tumour cannot be assessed

R0 No residual tumour

R1 Microscopic residual tumour

R2 Macroscopic residual tumour

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumour involving the resection margin on pathologic examination may be assumed to correspond to residual tumour in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

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