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Data Sets for the Reporting of Head and Neck Tumors

Second Edition Update From the International Collaboration of Cancer Reporting

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• ***Context.***—**The International Collaboration on Cancer Reporting is a not-for-profit organization whose goal is to develop evidence-based, internationally agreed standardized data sets for each anatomic site to be used throughout the world.**

Objective.—**To update the changes in the 2nd edition of the data set suite, including carcinomas of the hypopharynx, larynx and trachea, major salivary glands, nasal cavity and paranasal sinuses, oropharynx and nasopharynx, and oral cavity, and ear and temporal bone tumors, malignant odontogenic tumors, mucosal melanomas of the head and neck, and nodal excisions and neck dissection specimens.**

Design.—**International consensus by expert data set authoring committees, especially authors of the World Health Organization head and neck tumor classification.**

Results.—**The unique features have been updated based on current research and developments in histologic classification and standardized reporting guidelines. Separation between core and noncore elements is based on data meaningful to prognosis and stratification. The changes are in conjunction with publication of the 5th edition of the World Health Organization head and neck tumor classification.**

Conclusions.—**Increased harmonization of reporting and benchmarking improves patient outcomes and international collaborative research.**

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The International Collaboration on Cancer Reporting (ICCR) has developed data sets for various organ systems since 2011. This 2nd edition of the head and neck pathology reporting data sets, supported by several international colleges and organizations, was developed by an expert panel of data set authoring committee members for each anatomic site, including mucosal melanoma and neck lymph nodes. Lymphomas, skin tumors, and sarcomas are dealt with in separate data sets. The membership was composed of pathologists, oncologists, dentists, radiologists, and surgeons, all providing unique insight into head and neck tumor management. Pathologists are encouraged to use linked data sets to include all parameters of reporting and management. The expert panel distinguished between reporting of core elements and noncore elements, with core elements considered essential for clinical management, staging, or prognosis of the cancer based upon level III-2 or higher evidentiary support (based on prognostic factors in the National Health and Medical Research Council levels of evidence).[1] Noncore elements were agreed upon as clinically important and recommended as good clinical practice. This review will summarize the ICCR head and neck data set reporting guidelines for all the major anatomic sites, along with mucosal melanoma and nodal dissections. The ICCR data set includes the minimum reporting requirements for each site while providing the flexibility to include additional elements that may be needed at the local level. There is significant variation in the strength of the evidence available, because many of the anatomic sites have a low frequency of tumors. The ICCR head and neck data sets may be accessed freely at https://www.iccr-cancer.org/datasets/published-datasets/head-neck/. The Table delineates the 9 data sets of head and neck tumors and whether any changes occurred between editions to reporting by anatomic category and associated specific components.

DATA SET ELEMENTS UPDATED BY ANATOMIC SITE

Across all of the data sets, a new or updated element, clinical information, was added, specifically to include

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Updated Elements										
Category	Specific Components	Nasal Cavity and Paranasal Sinuses	Oropharynx and Nasopharynx	Oral Cavity	Hypopharynx, Larynx, and Trachea	Major Salivary Glands	Odontogenic	Ear and Temporal Bone	Mucosal Melanoma	Nodal Excisions and Neck Dissection
Clinical information		C	C	C	C	C	C	C	C	C
	Previous therapy (surgery, chemotherapy,radiotherapy, targeted therapy)	NC	NC	NC	NC	NC	NC	NC	C	NC
	Clinical staging	—	—	—	NC	—	—	—	—	NC
	Other clinical information	NC	NC	NC	NC	NC	NC	—	C	NC
Operative procedure		C	C	C	C	C	—	C	C	NC
Specimen(s) submitted	Specific list and other	C	C	C	C	C	C	C	C	C
Tumor site	Not specified, specific site listed, other specified	C	C	C	C	C	C		C	
Tumor laterality		C	C	C	C	C	C	C	C	C
Tumor focality		—	—	NC	C	NC	—	NC	—	—
Tumor dimensions		NC	C	C	C, NC	C	C	NC	NC	—
Histologic tumor type	List selection	C	C	C	C	C	C	C	C, NC	C
Histologic tumor grade	Not applicable, grade 1, 2 or 3, undifferentiated, high-grade transformation (grading system used)	C	C	C	C	C	C	C	—	C
Extent of invasion	Not identified, present (clinical, imaging, histologic), list features, cannot be assessed	C	C	C	C	C	NC	C	C	
Lymphovascular invasion	Not identified, present, indeterminate	C	C	C	C	C	NC	C	NC	
Perineural invasion	Not identified, present (nerve size or named nerve), indeterminate	C	C, NC	C	C	C	C	C	NC	
Margin status	Involved by invasive tumor (distance to closest margin)	C	C	C	C	C	C	C	NC	C
	Not involved by invasive tumor	C	C	C	C	C	C	C	NC	C
	Involved by CIS/dysplasia	—	C, NC	C	C	—	—	—	NC	—
	Not involved by CIS/dysplasia	—	C, NC	C	C	—	—	—	NC	—
Other/coexistent pathology		—	NC	NC	NC	NC	—	NC	NC	NC
Ancillary studies	List performed test(s)	C, NC	C, NC	C, NC	C, NC	C, NC	NC	C, NC	NC	C, NC
Representative block for ancillary studies		NC	NC	NC	NC	NC	NC	NC	NC	NC
Unique feature(s)		Precursor lesion(s) (C)		Depth of invasion (C) Pattern of invasive front (C)	Pattern of invasive front (NC) Precursor lesion(s) (NC)		Necrosis (C)		Necrosis (NC) Posttherapy changes (NC)	Specific lymph node level involved, largest metastatic size, size of lymph node affected, extranodal extension, soft tissue metastasis, and non-lymphoid structures involved Sentinel lymph node

Abbreviations: C, core; NC, noncore; CIS, carcinoma in situ.

previous therapy: surgery, chemotherapy, radiotherapy, and/or targeted therapy. Additionally, all data sets had 2 noncore elements added: block identification key and representative blocks for ancillary studies. The origin/designation of all tissue blocks should be included, providing an unequivocal description of the origin of each block to aid specialist opinion and facilitate block retrieval for ancillary testing, research studies, or clinical trials. A digital image of the specimen with tumor block key is encouraged. Further, specification of which blocks best represent tumor and/or normal tissue for further studies establishes good laboratory practice.

Carcinomas of the Nasal Cavity and Paranasal Sinuses

The changes in this data set are several, although none are major.[2] The operative procedure element was updated to allow the pathologist to indicate whether a resection was en bloc and open or piecemeal and endoscopic, with the latter being much more common. The specimens submitted element was modified slightly to include specific options for paranasal sinus and nasal cavity subsites. Tumor site was updated to remove laterality and make tumor laterality a separate new element. Tumor focality was removed, because multifocality in this site would be extremely unusual.

The most major changes involved updating the histologic tumor type element to reflect the most recent 2024 World Health Organization (WHO) classification.[3] SWI/SNF complex–deficient sinonasal carcinoma is a group that includes SWI/SNF related BAF chromatin remodeling complex subunit B1 (*SMARCB1*)–deficient and SWI/SNF related BAF chromatin remodeling complex subunit ATPase 4 (*SMARCA4*)–deficient sinonasal carcinomas, aggressive malignancies defined by their loss of specific proteins in the SWI/SNF complex.[4–7] Human papillomavirus (HPV)–related multiphenotypic sinonasal carcinoma is a newly recognized tumor that histologically mimics adenoid cystic carcinoma yet behaves more similarly to HPV-associated squamous cell carcinoma (SCC).[8,9] Teratocarcinosarcoma is now included in the data set; although not new, it is becoming more recognized as its genetics become better understood.[10]

Histologic tumor grade has been updated to include differentiation and grade as synonyms, as well as to include a high-grade transformation option. A new element, extent of invasion, has been updated, including the former bone/cartilage invasion, along with invasion of skin, skull base, and orbital tissues. Margin status was updated to remove the distance to margin option, in recognition that in most cases it is impossible to measure this distance. Coexistent pathology was replaced by precursor lesion. Ancillary studies was updated with ancillary studies options specifically listed, especially when they are tumor defining (Figure 1).

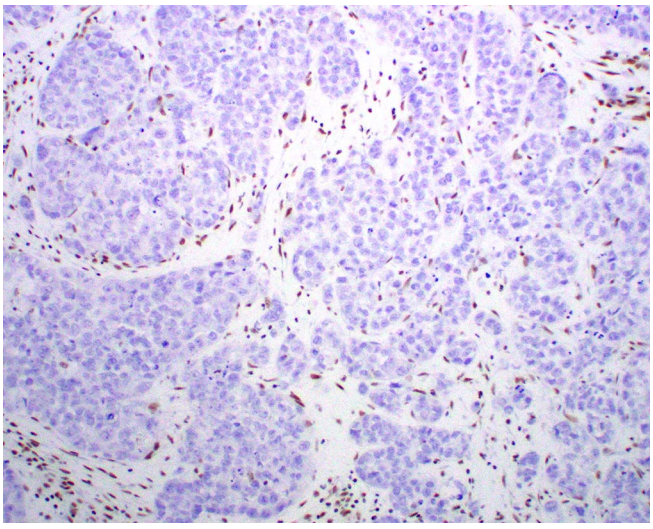


Figure 1. *SWI/SNF complex–deficient carcinoma is recognized as a carcinoma subtype uniquely defined by loss of SWI/SNF related BAF chromatin remodeling complex subunit B1 (*SMARCB1*) or SWI/SNF related BAF chromatin remodeling complex subunit ATPase 4 (*SMARCA4*) (most frequently). The neoplastic cells lack INI1 in this example of a* SMARCB1*-deficient sinonasal carcinoma, whereas fibroblasts and endothelial cells retain expression (INI1 immunohistochemistry, original magnification ×400).*

Carcinomas of the Oropharynx and Nasopharynx

The 2nd edition incorporates the 2024 WHO classification of head and neck tumors 5th edition[3] with revisions to the notes reflecting consensus opinion among the authors.[11] The data set is applicable to primary malignancies of the oropharynx and nasopharynx, including neuroendocrine neoplasms and minor salivary gland carcinomas, but does not apply to recurrent disease, lymphomas, sarcomas, or mucosal melanomas. For cases in which only a biopsy specimen is available, the data set elements specific to the biopsy should be reported, excluding those considered part of a resected specimen. For SCC from the oropharynx with synchronous or metachronous primaries, each separate tumor must have its own data set[12]; by contrast, multifocal tumors of the nasopharynx are reported using one data set.

In both the oropharynx and nasopharynx, neoadjuvant therapy with primary chemoradiation is the most common first-line therapeutic approach. Still, pathologic treatment response is not well established in the oropharynx[13] and does not seem to be significant in the nasopharynx.[14]

The tumor site element must include the specific portion of the pharynx, as there are implications for T classification and patient management. For patients with oropharyngeal carcinomas, the anatomic subsite within the oropharynx may provide information about the likelihood of high-risk HPV association.[15] Tumor laterality is also included.

The histologic tumor type is based upon classification of oropharyngeal and nasopharyngeal tumors according to the most recent edition of the WHO classification of head and neck tumors.[3] Oropharyngeal carcinomas are classified as HPV-associated or HPV-independent (Figure 2). Nasopharyngeal carcinomas are placed into 4 categories: low-grade nasopharyngeal papillary adenocarcinoma, keratinizing SCC, nonkeratinizing SCC (Figure 3), or basaloid SCC. Other options for histologic tumor type include salivary gland–type carcinomas, neuroendocrine neoplasms, and "other."

The histologic tumor grade element was updated to reflect grading of neuroendocrine neoplasms that include neuroendocrine tumors (NETs) grade 1, 2, 3, and neuroendocrine carcinomas (NECs), all by definition high grade. The grading is based upon mitotic rate and Ki-67 proliferation index as well as other factors. Furthermore, the histologic tumor grade is applicable to conventional HPV-independent and Epstein-Barr virus (EBV)–independent tumors and to salivary gland tumors.

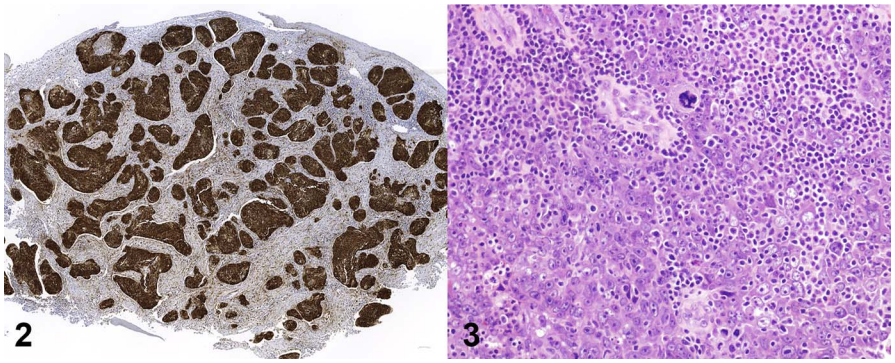


Figure 2. *An oropharyngeal carcinoma identified below the surface in the crypt epithelium shows a strong and diffuse nuclear and cytoplasmic immunoreaction for p16 in a block-type pattern in >95% of the neoplastic cells, even though >70% is the cutoff (p16 immunohistochemistry, original magnification ×12).*

Figure 3. *A nonkeratinizing nasopharyngeal carcinoma shows a syncytium of large pleomorphic neoplastic cells with prominent nucleoli (hematoxylin-eosin, original magnification ×400).*

The depth of invasion element was removed, as it is not prognostically meaningful, especially for HPV- and EBV-associated SCCs, because the tumors typically arise deep within the crypt mucosa (Figure 2) without an accurately obtained depth of invasion.

Extent of invasion was added, and includes "not identified," "present (specify)," and "cannot be assessed (specify)." For carcinomas of the oropharynx, the combination of tumor size and extent determine the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC) pT category.[15,16] For example, extension of the oropharyngeal carcinoma to the lingual surface of the epiglottis leads to a classification as pT3. For carcinomas of the nasopharynx, the tumor extent alone is used to determine the UICC and AJCC pT category.

The noncore coexistent pathology element was updated to "none identified" or "present." For the latter, specific information about the coexistent pathology can be entered by free text. Furthermore, several minor adjustments were made to ancillary studies used for categorization of oropharyngeal and nasopharyngeal neuroendocrine neoplasms. Within the data set, the pathologist should specify the neuroendocrine markers used, the cytokeratins used, and the Ki-67 proliferation index. In addition, information about the Rb status (retained versus deficient) and p53 status can be provided when performed.

Carcinomas of the Hypopharynx, Larynx, and Trachea

The 2nd edition incorporates several new elements.[17] In cases of previous treatment, clinical information must include the initial stage of the disease or at least information about vocal cord mobility. A digital image (photograph) of the specimen is highly recommended (Figure 4), irrespective of which data sets are being reported, but highlighted here. If this information is not included in the final pathology report, it should be available on the laboratory computer system. The definition of tumor focality and multicentricity was added to enable proper characterization of multiple primary tumors: *multifocal tumors* are defined as separate foci of tumors in the same organ, whereas *multicentric tumors* refers to multiple tumors in separate organs.

SCC remains the most common tumor of the larynx, hypopharynx, and trachea. It is still graded as well, moderately, or poorly differentiated SCC (Figure 5), despite limited prognostic significance. Approximately 10% of SCCs are subtypes, including verrucous carcinoma, basaloid SCC, papillary SCC, spindle cell SCC, acantholytic, adenosquamous carcinoma, and lymphoepithelial carcinoma. These are not graded; each subtype has its own intrinsic biological potential.[18]

Neuroendocrine epithelial neoplasms are rare in the head and neck sites in general, even though most common in the larynx, hypopharynx, and trachea (thus described here). They should be classified according to the unified WHO/International Agency for Research on Cancer terminology[19] as NETs, NECs, or mixed neuroendocrine-nonneuroendocrine neoplasms (MiNENs). NETs are well-differentiated tumors subclassified as NET grade 1, 2 or 3 based on morphology, number of mitoses per 2 mm^2, and the Ki-67 proliferation index. The diagnosis of NEC should be used only for poorly differentiated neuroendocrine neoplasms, further classified as either small cell or large cell NECs. Differentiating NET grade 3 from NEC may be difficult, but immunohistochemistry for Rb and p53 is recommended in ambiguous cases: loss of expression of Rb and aberrant expression of p53 favor the diagnosis of NEC.[20,21] MiNENs are usually composed of NET or NEC and SCC or adenocarcinoma; tumor components must be confirmed immunohistochemically and reported irrespective of their extent. Tumor budding determined at the invasive front is a potential prognostic parameter in SCC of the head and neck in general, and specifically oral cavity, larynx, and hypopharynx, but there is no consensus yet on how it should be assessed and graded.[22] Conceptually, a tumor bud is defined as a continuous phenomenon in which single cells and isolated tumor cell clusters (up to 4 cancer cells) detach from the main tumor invasive front and invade into the adjacent stroma. The numbers of buds in areas showing maximal budding are counted, normalized to a field of 0.785 mm^2 (×20 objective with eyepiece diameter of 20 mm), and a 2-tier scoring system is adopted with a cutoff point of 5 buds (low risk <5 buds versus high risk ≥ 5 buds). Generally, the cutoff of 5 or more buds seems to be an appropriate discriminator to stratify patients without use of ancillary testing.[23] As such, the extent of invasion was emphasized especially for SCC.

Recently, anti–PD-1 antibodies nivolumab and pembrolizumab were the first immune checkpoint inhibitors approved for the treatment of patients with recurrent and/or unresectable metastatic head and neck SCC.[24,25] One factor that may help to predict the response to treatment is the expression of programmed death ligand-1 (PD-L1) on tumor and immune cells. To assess the expression of PD-L1 in SCC of the head and neck, it is currently advised to calculate a combined positive score (CPS) based on immunohistochemistry using antibody 22C3. CPS is defined as the number of PD-L1–positive cells (tumor cells, lymphocytes, and macrophages) divided by the total number of tumor cells × 100.

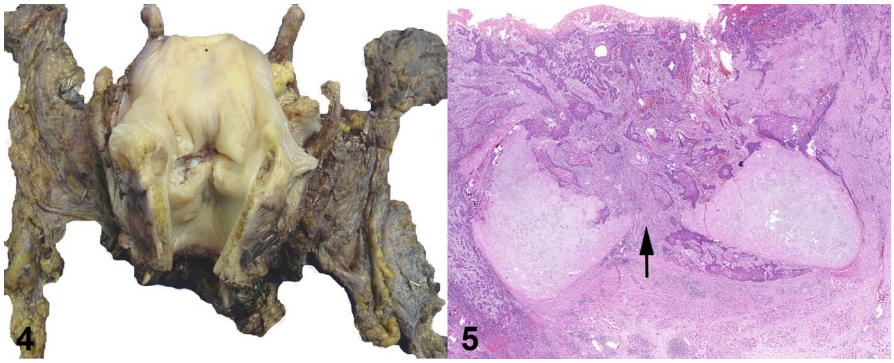


Figure 4. *A photograph of gross total laryngectomy specimen with a transglottic squamous cell carcinoma (courtesy Jason C. Fowler, MPAS, PA-C).*

Figure 5. *A moderately differentiated keratinizing squamous cell carcinoma deeply invading into the cartilage (black arrow) of a transglottic tumor (hematoxylin-eosin, original magnification ×20).*

Although CPS scores are variable, a CPS of 1 or higher is associated with better responses.[26,27]

p16 immunohistochemistry as a surrogate marker for HPV-associated SCC may be less reliable in the larynx and hypopharynx than in the oropharynx.[28,29] A higher proportion of laryngeal SCC overexpresses p16 but is HPV independent compared with other head and neck sites,[28] primarily because high-risk HPV infection is a rare cause of larynx and hypopharynx SCC when determined by high-risk HPV E6/E7 mRNA in situ hybridization. Still, testing is encouraged, particularly in cases with basaloid, papillary, lymphoepithelial, or warty morphology.[30,31]

Carcinomas of the Major Salivary Glands

Several new elements were included in the 2nd edition, including new findings along with updates and clarification for most of the data values.[32]

Three new elements were clinical information, tumor laterality, and block identification key, along with a complete update of the histologic tumor type based on publication of the WHO 5th edition head and neck tumor classification.[33]

Tumor laterality became a separate element rather than part of the tumor site, an important characteristic for oncologic quality assurance and follow-up management about side/site-specific treatment.[34,35] Ancillary testing is being conducted more commonly for diagnostic and prognostic information (Figure 6), with several genetic alterations seen in benign tumors also retained in malignant counterparts, a consideration important in tumor classification.

Neck dissection along with other specimen parts were added to the specimen(s) submitted element, reducing the number of specimens to checkbox entries.[36] The histologic tumor type originally included grading within each entity, making for a tedious and cumbersome entry.[37] Histologic tumor grade has been expanded to include grades 1 through 3, undifferentiated and high-grade transformation, with a free-text box to enter the specific grading system used, rather than forcing the use of one grading scheme.[38] The extent of invasion was expanded to include clinical observation (including intraoperative) and/or imaging findings along with histologic features to document invasion, as many times the clinical or imaging findings show nerve or vessel involvement or even bone destruction that may not have been included in the histologic samples submitted (Figure 6). Several minor but important changes included adding the category of "indeterminate" to several of the elements, with free-text fields to explain why the feature could not be placed in either "not identified" or "present," findings frequently determined by sample type or other technical limitations; changing the order for margin status was changed to list "not involved" first, then followed by "involved by invasive carcinoma;" adding specific coexistent pathology findings, although a free text "other [specify]" category remained; and separating ancillary studies into immunohistochemistry/in situ hybridization and molecular markers, leaving free-text space to specify the test performed and the results obtained. The specific rationale and support for each of these changes was included in the supporting notes, while keeping the AJCC/UICC 8th edition staging.[15,16]

Carcinomas of the Oral Cavity

This edition reflects updates from the 5th edition of the WHO classification of head and neck tumors,[3] with subtypes of oral SCC (OSCC) remaining the same, but removing "cannot be assessed." This data set applies to primary malignancies of the oral cavity, including mucosal carcinomas, minor salivary gland malignancies, and neuroendocrine neoplasms.[39] Neck

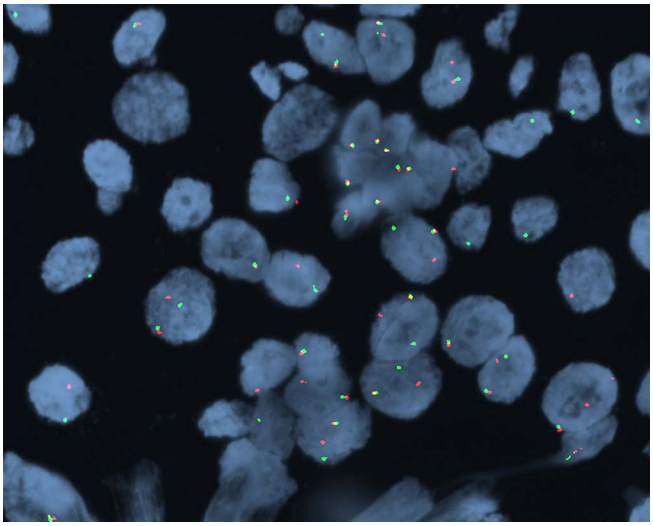


Figure 6. *A tongue mucoepidermoid carcinoma would be supported by mastermind-like transcriptional coactivator 2 (*MAML2*) break-apart fluorescence in situ hybridization (FISH) as an ancillary technique. A break-apart FISH probe for* MAML2 *has 2 fluorescently labeled DNA sequences flanking the 5′ end and the 3′ end of the* MAML2 *gene. In cells with rearrangement, there will be a distinct orange and green signal reflecting the break (normal cells have a single yellow fusion signal) (original magnification ×600).*

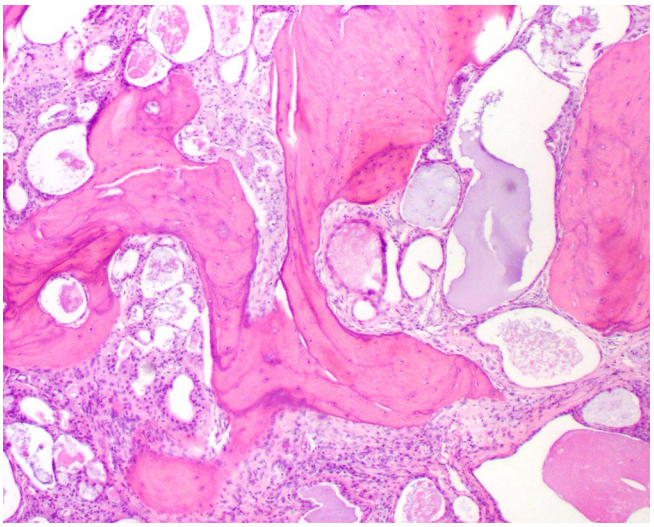


Figure 7. *Destructive infiltration by a squamous cell carcinoma into deep bony interstices (hematoxylin-eosin, original magnification ×300).*

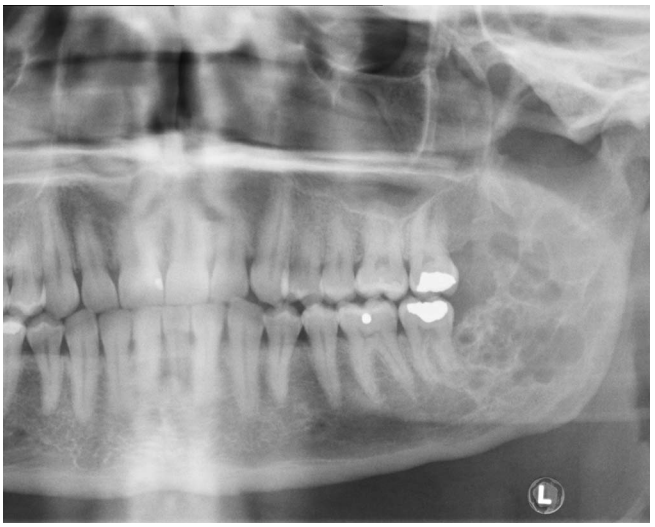


Figure 8. *Radiologic correlation with the histologic findings is mandatory. A left mandibular body and ramus ameloblastoma shows a bubbly radiolucency in this orthopantomograph.*

dissections/nodal excisions, mucosal melanoma, sarcomas, and lymphomas are reported separately.

Clinical information is a new element, incorporating the previous element neoadjuvant therapy. Despite no agreed-upon system for grading tumor regression in OSCC, histologic changes may result from previous therapy, which may impact tumor assessment,[40] with response to neoadjuvant therapy removed. The tumor site element reflects that the vermilion border of the lip is of cutaneous origin and only mucosal (wet) lip carcinomas are OSCC.[41] In addition, the section is streamlined by creating a separate tumor laterality element.

The tumor dimensions element no longer includes maximum depth of invasion, as this is more accurately measured microscopically and not on the tumor specimen.[16] In contrast to the 1st edition, wherein only conventional OSCC was graded, grading applies to OSCC, minor salivary gland tumors, and NETs, the latter restricted to grade 1, 2 and 3, as NECs are high grade and not graded.[42]

"Extent of invasion" replaced "bone invasion" (Figure 7), recognizing that destructive infiltration of bone by OSCC is associated with a worse prognosis and affects tumor staging,[43] but other elements like maxillary sinus involvement and skin involvement were also added. Margin status was updated to include WHO 5th edition terminology,[3] documenting carcinoma in situ/high-grade dysplasia at margins and distance to the closest margin (high-grade dysplasia is synonymous with moderate/severe dysplasia).[44] Ancillary studies was expanded to include studies required to diagnose and correctly grade NETs.

Malignant Odontogenic Tumors

There are relatively few changes to the data set for malignant odontogenic tumors, most having been introduced for consistency across the series.[45] The changes are primarily noncore and, as in other tumor groups, now include previous targeted treatments in the clinical information section and the separation of tumor laterality. Specific changes relevant to odontogenic tumors are the addition of a possible extraosseous origin and that a tumor grade is now a requirement for primary intraosseous carcinoma, when previously it was possible to select "not applicable." Grading remains applicable only to primary intraosseous carcinoma.

The diagnostic categories have not required any updating to the WHO 2024 classification, because this is unchanged from the previous edition; only the order is changed to reflect increasing malignancy. Additional evidence confirming the malignant nature of sclerosing odontogenic carcinoma is now noted,[46] but other contentious entities such as odontogenic carcinosarcoma, which is poorly defined, remain pending changes to the classification.

All odontogenic tumors are rare, and malignant tumor types particularly so. The 1st edition of the data set was heavily based on professional opinion, but some new data have been published to refine the data set,[47–49] though no new scoring or grading systems or features have been added. Some new systematic reviews support the existing data set items,[50,51] but there remains a lack of high-level evidence to support the data set.

Although the molecular basis of odontogenic tumors is increasingly defined, there are only sparse data on malignant odontogenic tumors, and few changes are targetable. B-Raf proto-oncogene, serine/threonine kinase (*BRAF*) p.V600E sequence variation is found in many benign ameloblastomas (Figure 8), in other odontogenic tumors with an ameloblastic component, and in some malignant odontogenic tumors. Targeted therapy has proved very successful in benign ameloblastoma, but data for malignant odontogenic tumors remain limited.[52,53] The new data set includes BRAF assessment in the ancillary studies element and requires the method to be specified, because immunohistochemical analysis of odontogenic tumors is a poor surrogate for sequencing.[54,55] It is hoped that the new opportunity to allow selection of the best block for subsequent studies and the block identification key will facilitate further research into targetable molecular changes, as

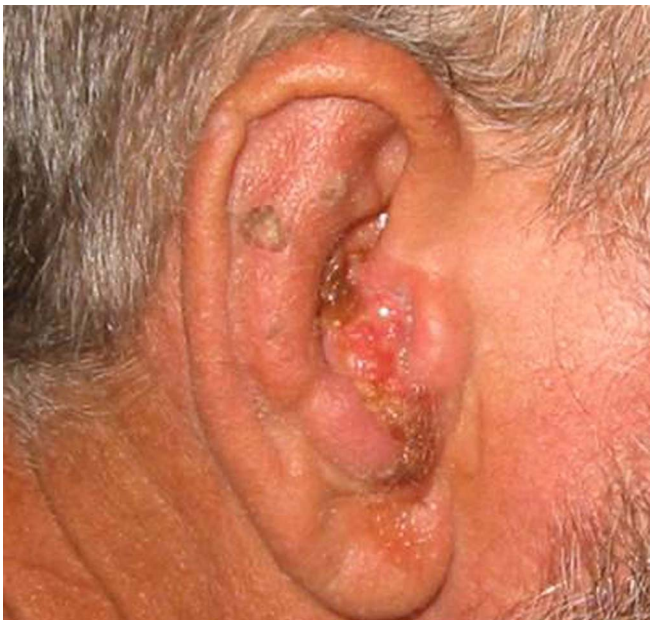


Figure 9. *A clinical photo of a right external auditory canal squamous cell carcinoma (courtesy Carsten E. Palme, MBBS, FRACS).*

decalcification often renders odontogenic tumors unsuitable for analysis.

Ear and Temporal Bone Tumors

There is still no standardized AJCC/UICC staging system for ear and temporal bone tumors, and so this reporting guide continues to play a critical role in reporting them.[56] This anatomic area is exceptionally complex and compact, with similar surgeries for both benign and malignant neoplasms; therefore, both benign and malignant tumors are covered by this data set, recognizing a multidisciplinary approach to management. Specific new elements include tumor laterality with updated reporting suggestions for the remaining elements, moving some from noncore to core or vice versa.

Core biopsies or incisional biopsies are frequently performed as diagnostic procedures but may result in alterations to the tissue at the time of resection. For this reason, including clinical information, especially about previous therapies (surgery, chemotherapy, radiation, targeted or immunotherapy) will aid in interpretation, and other clinical information about history, concurrent findings, imaging, or genetic evaluations will help with diagnosis and prognostication. As for other anatomic sites, tumor laterality was extracted as its own element as an important oncologic parameter[57] (Figure 9).

The updates to the operative procedure element include a more robust definition of the types of temporal bone resections (sleeve, cortical, lateral temporal bone, subtotal temporal bone, and total temporal bone resections) and placing them in order of progressively more radical procedures, recognizing that different terminology may be used locoregionally; this is an attempt at harmonization.[58] The specimen(s) submitted and tumor site elements followed the same update.[59]

Tumor dimensions are not as critical as the sites affected, and thus the extent of invasion element includes clinical, imaging, and/or histologic findings of skin, bone, dura, brain, parotid gland and soft tissue involvement (the latter including dimensions used for staging).[60–62] The histologic tumor type was updated based on the 5th edition of the World Health Organization head and neck tumor classification,[63] recognizing NETs along with several benign neoplasms that can result in significant local destruction and thus "oncologic" management. Tumor grading is applicable only to SCC and NETs, but standardized grading terms were applied to this element, recognizing that reported case numbers are small and thus good prognostication separation is not yet uniformly applicable.[64]

Several elements had "indeterminate" free text added to explain why a feature was either not identified or present. Limitations of the sample type, decalcification, fragmentation, frozen section artifacts, etc, potentially preclude assessment. The order of margin status reporting was changed to "not involved" and then "involved by invasive" carcinoma. Coexistent pathology findings may limit follow-up treatment options and so were included as noncore elements.[65] The ancillary studies element specifically added studies for neuroendocrine neoplasm assessment along with a Ki-67 proliferation index, elements generally considered necessary in accurate classification.[66] All supporting notes were carefully updated to include a reflection of the current literature and most recent updates in the classification system.

Mucosal Melanomas of the Head and Neck

The mucosal melanomas data set provides a contemporary reporting structure to be used for biopsy and resection specimen of mucosal melanomas arising in the nasal cavity, paranasal sinuses, oral cavity, and any region of the pharynx or larynx.[67] Mucosal melanomas of the upper aerodigestive tract are rare, at 1% to 2% of all melanomas diagnosed[68]. Previous studies have shown that mucosal melanomas diverge from cutaneous melanomas with unknown etiologic factors and differences in prognostic and molecular profiles.[69,70] Cutaneous melanomas are reported with the ICCR invasive melanoma reporting data set,[71] but conjunctival, uveal, and retinal melanomas are beyond the scope of this data set.

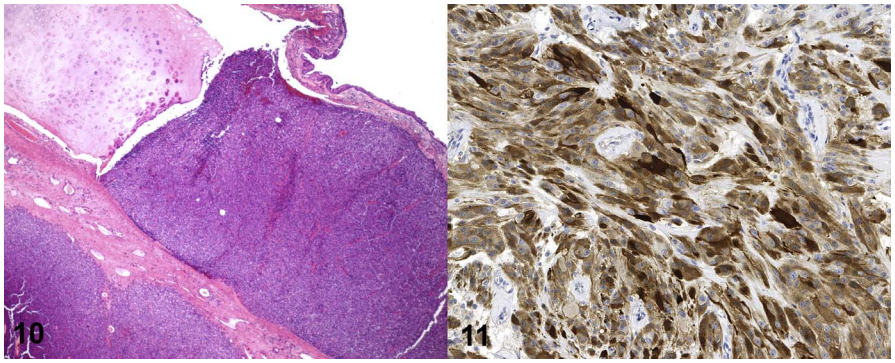
In the 2nd edition, elements recorded are expanded, harmonizing the pathologic features captured across the head and neck data set suite. Each element is detailed in the ICCR's accompanying histology reporting guide for the data set with supporting literature references (Figure 10). Examples of noncore elements now incorporated are perineural invasion and lymphovascular invasion as discrete elements.

As therapeutic considerations continue to evolve, capturing the associated clinical information of previous therapy is essential for evaluation and staging and is a core element. Previous therapy in mucosal melanoma may include surgery, radiation, chemotherapy, targeted therapy, or immunotherapy.[69,72] These factors allow for ypTNM. Corresponding histologic elements added include recording posttherapy changes when applicable as response or no response and providing percentage tumor viability. Necrosis, as present or absent, is also now separately recorded.

Another key feature for staging is the extent of tumor invasion. The histologic features corresponding to each T category are now clearly delineated for easier determination. As mucosal

Figure 10. *A sinonasal tract mucosal melanoma demonstrates cartilaginous destructive infiltration (hematoxylin-eosin, original magnification ×12).*

Figure 11. *Several immunohistochemistry studies are useful in supporting a diagnosis of melanoma, with S100 protein one of the most frequently used (original magnification ×400).*



melanoma's overall prognosis is poor (<31% 5-year overall survival),[72,73] no tumors are classified pathologically as pT1 or pT2. Thus, when mucosal melanomas are limited to the mucosa and/or submucosa, they are within pT3. As tumors show moderately advanced invasion (pT4a), anatomic tissues invaded include deep soft tissues, muscle, cartilage (Figure 10), bone, and/or underlying skin. With very advanced mucosal melanomas (pT4b), tumor invasion extends to the skull base or intracranial structures (brain or dura) or lower cranial nerves (IX, X, XI, XII), invades the masticator or prevertebral space, extends to the mediastinum, or encases the carotid artery.[15,16]

For histologic tumor type, terminology was updated to align with the 5th edition WHO classification of head and neck tumors, for which mucosal melanomas may be further characterized as lentiginous, nodular, and desmoplastic subtypes as a noncore element.[3] A representative block for ancillary studies is identified in the report (Figure 11).

Nodal Excisions and Neck Dissection Specimens

Primary tumor site was changed from a noncore to core element in this 2nd edition.[74] If known, this is considered necessary information, particularly as nodal excisions/neck dissections may not be accompanied by the primary tumor resection. The histologic tumor types were updated to match the 2024 WHO Classification of Head and Neck Tumours.[3] The NET entry was simplified to a single component, "neuroendocrine neoplasm, specify type." This will cover the broad range of neuroendocrine neoplasms from multiple sites in the head and neck without requiring an exhaustive list of all possible primary tumor sites and subtypes of neoplasms (NETs, NECs, MiNENs).

Margin status of the neck dissection specimen was changed from a noncore to a core element, and adjustments to subcomponents of this section were made to improve the targeting of postoperative radiotherapy treatment.[75–79] For those cases with a negative margin, the site of the closest margin was added. For those cases with a positive margin, specification of the lymph node compartment(s) involved is now required, in addition to just the laterality. The panel recommends applying ink to neck dissection specimens with a palpable tumor mass in which extranodal extension is suspected or cannot be excluded. If a specimen is not inked and tumor is entirely intranodal, it is reasonable to report the margin as not involved by carcinoma, without providing a distance to the margin.

Ancillary studies is now a core element, with specific reference to HPV and EBV testing results and methods. HPV testing, whether via surrogate p16 status (Figure 12) or an HPV-specific method, is necessary for correct management of oropharyngeal SCC in particular.[80] EBV testing is required to correctly diagnose nasopharyngeal carcinoma in a neck mass.[81]

Some components of the lymph node status element have been altered. The number of nodes with extranodal extension—previously a noncore element—was removed, as the expert panel did not have evidence to support its continued inclusion with respect to patient management. Nonlymphatic structures involved was changed from a noncore to a core element, with the requirement to specify named nerves, muscles, or blood vessels, when known. This change was made to provide additional information for adjuvant treatment planning.[79]

A sentinel lymph node biopsy noncore element was added to reflect the growing importance of this technique for accurate staging of the neck in oral cavity SCC.[72,82,83] The expert panel recommended subcategorization of the size of metastatic tumor deposits in sentinel lymph nodes into isolated tumor cells, micrometastasis, and metastasis. The expert panel did not specify the optimal assessment method for sentinel nodes (for example via frozen section, extent of sampling, or use of immunohistochemistry), as

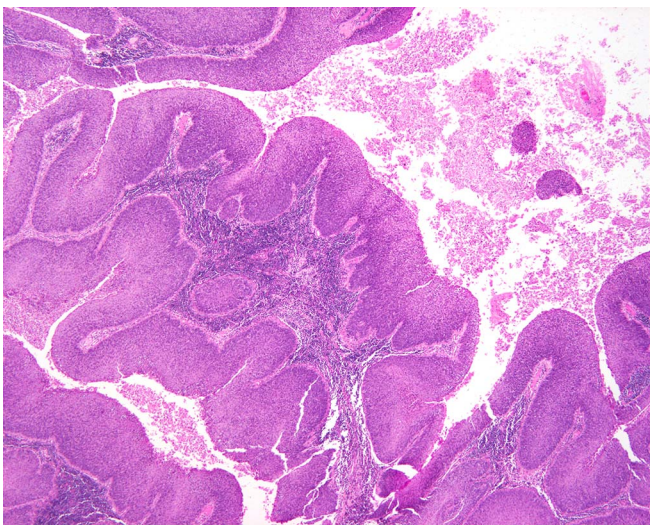


Figure 12. *Metastatic oropharyngeal carcinoma showing a ribbonlike and endophytic growth (hematoxylin-eosin, original magnification ×40).*

variability exists among centers that practice sentinel lymph node biopsy.[83]

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