

# Carcinomas of the Nasal Cavity and Paranasal Sinuses 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**. indicates multi-select values  indicates single select values

SCOPE OF THIS DATASET

**CLINICAL INFORMATION** (Note 1)

- Information not provided  
 Information provided (select all that apply)

 Previous therapy

- Surgery  
 Chemotherapy  
 Radiotherapy

 Targeted therapy, *specify if available* Immunotherapy, *specify if available* Other clinical information, *specify***OPERATIVE PROCEDURE** (select all that apply) (Note 2)

- Not submitted  
 Biopsy (excision, incisional, core needle), *specify*

 Resection

- Open  En bloc  
 Endoscopic  Piecemeal  
 Combined

 Neck (lymph node) dissection,<sup>a</sup> *specify* Other, *specify*<sup>a</sup> If a *neck (lymph node) dissection* is submitted, then a separate dataset is used to record the information.**SPECIMEN(S) SUBMITTED** (select all that apply) (Note 3)

- Not specified  
 Nasal cavity, *specify*

 Paranasal sinus(es), *specify* Orbit, *specify* Neck (lymph node) dissection,<sup>a</sup> *specify* Other, *specify***TUMOUR SITE** (select all that apply) (Note 4)

- Not specified  
 Nasal cavity  
 Septum  Lateral wall  
 Floor  Vestibule  
 Paranasal sinus(es), maxillary  
 Paranasal sinus(es), ethmoid  
 Cribriform plate  
 Paranasal sinus(es), frontal  
 Paranasal sinus(es), sphenoid  
 Orbit  
 Cranial cavity  
 Other, *specify*

**TUMOUR LATERALITY** (select all that apply)

- Not specified  
 Left  
 Right  
 Midline

**TUMOUR DIMENSIONS** (Note 5)Maximum tumour dimension (largest tumour)  
(pathology and/or imaging determination) mm

Additional dimensions (largest tumour)

 mm ×  mm**BLOCK IDENTIFICATION KEY** (Note 6)*(List overleaf or separately with an indication of the nature and origin of all tissue blocks)*

**HISTOLOGICAL TUMOUR TYPE** (select all that apply) (Note 7)

(Value list based on the World Health Organization Classification of Head and Neck Tumours (2024))

- Keratinising squamous cell carcinoma
- Other squamous cell carcinoma subtype, *specify type*

- Non-keratinising squamous cell carcinoma
- NUT carcinoma
- SWI/SNF complex-deficient sinonasal carcinoma
- Sinonasal lymphoepithelial carcinoma
- Sinonasal undifferentiated carcinoma
- Teratocarcinosarcoma
- HPV-related multiphenotypic sinonasal carcinoma
- Adenocarcinoma

- Intestinal-type adenocarcinoma
- Non-intestinal-type adenocarcinoma

- Salivary gland-type carcinoma,<sup>b</sup> *specify type*

- Neuroendocrine neoplasm
  - Small cell neuroendocrine carcinoma
  - Large cell neuroendocrine carcinoma
  - Carcinoma mixed with neuroendocrine carcinoma

- Other, *specify*

<sup>b</sup> For histological type of salivary gland-type carcinomas, refer to the [Carcinomas of the major salivary glands](#) dataset.

**HISTOLOGICAL TUMOUR GRADE<sup>c</sup>** (Note 8)

(Not applicable to all tumours)

- Not applicable
- Grade 1, well differentiated, low grade
- Grade 2, moderately differentiated, intermediate grade
- Grade 3, poorly differentiated, high grade
- Undifferentiated
- High grade transformation

Grading system used, *specify*

- Cannot be assessed, *specify*

<sup>c</sup> Grading of neuroendocrine tumours is non-core. Use only Grade 1, 2 and 3 for neuroendocrine tumours; neuroendocrine carcinomas are considered high grade by definition and are therefore not graded.

**EXTENT OF INVASION** (Note 9)

- Not identified
- Present (select all that apply)

- Clinical observation and/or imaging
- Histologic

- Bone/cartilage invasion
  - Cortical bone erosion
  - Medullary bone involvement
- Soft tissue infiltration
- Skull base involvement
- Invasion of skin
- Invasion of orbital tissues

- Other, *specify*

- Cannot be assessed, *specify*

**LYMPHOVASCULAR INVASION** (Note 10)

- Not identified
- Present
- Indeterminate, *specify reason*

**PERINEURAL INVASION** (Note 11)

- Not identified
- Present
- Indeterminate, *specify reason*

**MARGIN STATUS** (Note 12)

- Not involved by invasive carcinoma
- Specify closest margin(s), if possible

- Involved by invasive carcinoma
- Specify margin(s), if possible

- Cannot be assessed, *specify*

**PRECURSOR LESIONS** (Note 13)

- Not applicable
- Not present
- Present (e.g., sinonasal papilloma (type), surface dysplasia), *specify*

**ANCILLARY STUDIES** (Note 14)

- Not performed
- Performed

If performed, specify (select) all that apply

**Non-keratinising squamous cell carcinoma**

- Positive
  - Pancytokeratin
  - p63
  - p40
  - CK5/6

- Negative
  - CD99
  - NKX2.2
  - NUT

- INI1
  - Retained
  - Deficient

- BRG1
  - Retained
  - Deficient

**NUT carcinoma**

- Positive
  - NUT immunohistochemistry
  - NUTM1 gene rearrangement, *specify technique*

**ANCILLARY STUDIES (Note 14) continued**

**SWI/SNF complex-deficient sinonasal carcinoma**

- INI1  
 Retained  Deficient
- BRG1  
 Retained  Deficient

**Sinonasal undifferentiated carcinoma**

- Positive  
 Pancytokeratin  CK7  
 IDH1/2
- Negative  
 p40/p63  NKX2.2  
 CK5/6  NUT  
 CD99
- INI1  
 Retained  Deficient
- BRG1  
 Retained  Deficient

**HPV-related multiphenotypic sinonasal carcinoma**

- Positive  
 p16 immunohistochemistry (screening)  
 HPV-specific testing, *specify technique*

**Neuroendocrine carcinoma**

- Positive  
 CAM5.2/CK-pan  Synaptophysin  
 Chromogranin  INSM1  
 Ki-67 proliferation index  %
- Rb  
 Retained  Deficient

**Keratinising squamous cell carcinoma**

- Positive  
 Pancytokeratin  p63  
 p40  CK5/6

**Sinonasal lymphoepithelial carcinoma**

- Positive  
 Pancytokeratin  EBER in situ hybridization  
 p16

**Teratocarcinosarcoma**

- Positive  
 Nuclear  $\beta$ -catenin
- BRG4 (SMARCA4)  
 Retained  Deficient

**Intestinal-type sinonasal adenocarcinoma**

- Positive  
 CDX2  SATB2  
 CK20  Villin  
 CK7

**Non-intestinal-type sinonasal adenocarcinoma**

- Positive  
 CK7  S100 protein  
 SOX10  Nuclear  $\beta$ -catenin  
 DOG1
- Negative  
 CK20  CDX2

**Other ancillary studies, record test(s), methodology and results**

**Representative blocks for ancillary studies, specify those blocks best representing tumour and/or normal tissue for further study**

**PATHOLOGICAL STAGING (UICC TNM 8<sup>th</sup> edition)<sup>d</sup> (Note 15)**

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

- m - multiple primary tumours  
 r - recurrent  
 y - during or following multimodality therapy

**Primary tumour (pT)<sup>e</sup>**

- TX<sup>f</sup> Primary tumour cannot be assessed  
 Tis Carcinoma in situ

**MAXILLARY SINUS**

- T1 Tumour limited to the mucosa with no erosion or destruction of bone
- T2 Tumour causing bone erosion or destruction, including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
- T3 Tumour invades any of the following: bone of posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, or ethmoid sinuses
- T4a Tumour invades any of the following: anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
- T4b Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

**NASAL CAVITY AND ETHMOID SINUS**

- T1 Tumour restricted to one subsite of nasal cavity or ethmoid sinus, with or without bony invasion
- T2 Tumour involves two subsites in a single site or extends to involve an adjacent site within the nasoethmoidal complex, with or without bony invasion
- T3 Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate
- T4a Tumour invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses
- T4b Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx, or clivus

<sup>d</sup> Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8<sup>th</sup> Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley (incorporating any errata published up until 12<sup>th</sup> July 2024).

<sup>e</sup> Note that the results of [neck \(lymph node\) dissection](#) are derived from a separate dataset.

<sup>f</sup> TX should be used only if absolutely necessary.

## Definitions

### CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence<sup>1</sup>). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

### NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of DAC.

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## Scope

The dataset has been developed for the reporting of resection and biopsy specimens of mucosal malignancies originating in the nasal cavities and paranasal sinuses. Malignancies at the border of skull base are included. Neuroendocrine neoplasms are also included.

Melanomas, lymphomas, sarcomas, olfactory neuroblastoma and haematolymphoid tumours are not included. Bone and soft tissue tumours are dealt with in separate ICCR datasets.

Neck dissections and nodal excisions are dealt with in a separate ICCR dataset, and this dataset should be used in conjunction, where applicable.<sup>2</sup>

This dataset is intended for use for primary cancer resections. For resections of recurrent disease, the reporting guide may be used pragmatically although some data elements may be not applicable nor assessable.

For additional independent tumours, complete a separate dataset for each.

The second edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Head and Neck Tumours, 5<sup>th</sup> edition, 2024.<sup>3</sup>

A list of changes in this dataset edition can be accessed [here](#).

The authors of this dataset can be accessed [here](#).

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## **Note 1 – Clinical information (Core and Non-core)**

Patients affected by locally advanced sinonasal carcinomas may be treated with pre-operative chemo-radiation protocols that could result in a significant improvement in survival in selected cases.<sup>4-7</sup>

In this case, specimens should be extensively sampled and changes presumably induced by treatment should be reported as free text (e.g., ‘with treatment effect’). Quantification of the extent of response is currently considered not relevant for clinical purposes. Type of therapy, number of cycles, interval between last cycle of chemotherapy and local regional treatment initiation can be annotated if available.

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## **Note 2 – Operative procedure (Core)**

Different options are currently available for the surgical treatment of sinonasal malignancies, which can be chosen according to histopathology, extent of the lesion, and experience of the surgeon. Surgical approaches include open craniofacial resections, endoscopic endonasal resections, and combined approaches.<sup>8-10</sup> This results in a wide range of surgical specimens submitted for histopathological analysis.

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## **Note 3 – Specimen(s) submitted (Core)**

According to the surgical approach, different types of specimen can be submitted for histological analysis. Specimens from surgery often consist of fragmented material that should be properly labelled at the time of surgery including a description of the anatomic site and type of tissue submitted (tumour or other). Due to the difficulty in the orientation of the samples (impossible in some cases) it is recommended that margins be submitted separately, properly identified and labelled (especially in suspicious areas). Surgical resection specimens consist most often of the maxillary bone and adjacent anatomic structures removed according to the extent of the tumour.<sup>11</sup>

Specimens from increasingly common endoscopic operations consist of fragmented material. Due to the difficulty in the orientation of such samples (impossible in some cases), it is recommended that margins be submitted separately, properly identified and labelled (especially in suspicious areas).

For additional independent tumours use separate datasets. A single bilateral tumour can be reported as 'midline'.

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## **Note 4 – Tumour site (Core)**

The sinonasal tract consists of the nasal cavity and the paranasal sinuses (maxillary, ethmoid, frontal, and sphenoid). The nasal cavity can be further subdivided into the nasal septum, floor, lateral wall, and vestibule. Among sinonasal tract carcinomas, the most common site of tumour origin is the maxillary sinus, followed by the nasal cavity and ethmoid sinus. It is rare for carcinomas to arise from the frontal or sphenoid sinuses, except for neuroendocrine tumours in the sphenoid or pituitary origin.<sup>12-16</sup>

The precise tumour site within the sinonasal tract is important to record. First, different staging schemes are utilised for maxillary sinus carcinomas and those arising in the ethmoid sinus or nasal cavity.<sup>17,18</sup> Second, there is prognostic importance to the tumour location. For example, carcinomas primary to the nasal cavity have been shown to have an improved prognosis over carcinomas primary to the paranasal sinuses, likely because nasal carcinomas give rise to symptoms (e.g., nasal obstruction or epistaxis) and thus come to clinical attention sooner.<sup>12,16,19,20</sup> In addition, among maxillary sinus carcinomas, those arising from the anterior-inferior portion have a better prognosis than those arising from the superior-posterior portion, likely because the latter group has easier access to structures such as the orbit or skull base.<sup>17,18</sup> Finally, certain carcinomas are closely associated with specific sinonasal sub-sites. For example, intestinal-type adenocarcinomas and neuroendocrine carcinomas occur most often in the ethmoid sinuses, while squamous cell carcinoma (SCC) occurs most often in the maxillary sinus.<sup>21-24</sup>

It is recognised that many carcinomas affect more than one sinonasal anatomic sub-site. In this case, every affected site should be selected.

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## **Note 5 – Tumour dimensions (Non-core)**

For en bloc resections, tumour size should be recorded based on gross examination of an unfixed specimen. In this anatomic site, however, tumour size does not affect staging. Moreover, due to the prevalence of endoscopic procedures resulting in fragmented specimens, it is often not possible to determine tumour size with accuracy. The option 'cannot be assessed' should be used in this scenario.

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## Note 6 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and is particularly important when further internal or external review arises. The reviewer needs to have unequivocal description of the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. It is highly encouraged to have a digital image (photograph) of the specimen and record of the key of the tumour blocks.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies, or clinical trials.

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## Note 7 – Histological tumour type (Core)

All sinonasal tumours should be classified based on the most recent edition of the WHO Classification of Head and Neck Tumours, 5<sup>th</sup> edition, 2024 (Table 1).<sup>3</sup> The list of histologic types discussed in the chapter on sinonasal tumours in the 5<sup>th</sup> edition of the WHO does not include salivary gland type tumours or neuroendocrine tumours because they are described in sections devoted to those topics. Tumours of these types should be reported using the this dataset, with reference to the ICCR Carcinomas of the major salivary glands dataset for guidance on histological typing.<sup>25</sup> Neuroendocrine neoplasms, specifically carcinomas (small cell and large cell) develop in this site and are recorded here. Neuroendocrine tumours grade 1 and 2 are vanishingly rare, and thus are not specifically included, but can be entered in ‘other’.

The sinonasal tract gives rise to a very large and diverse group of malignant tumours.

Accurate tumour typing is important because specific tumour types are associated with different prognoses and, in some cases, different treatments.

Diagnostic accuracy is also expected to take on additional importance in the future as targeted, molecular-based therapies become more prominent. While routine histologic examination has historically been the mainstay for diagnosis, an increasingly large number of sinonasal malignancies require ancillary testing to diagnose (see **NOTE 14 – ANCILLARY STUDIES**). Because these ancillary techniques are not universally available, a diagnosis of ‘Carcinoma, not otherwise specified’ with an explanatory comment may be given if a diagnosis cannot be further refined with the testing methods available to the pathologist.



**Table 1: World Health Organization classification of tumours of the nasal cavity, paranasal sinuses and skull base.<sup>3</sup>**

Descriptor	ICD-O codes <sup>a</sup>
<b>Carcinomas</b>	
Keratinising squamous cell carcinoma	8071/3
Other squamous cell carcinoma subtypes: Papillary, verrucous, spindle cell, acantholytic, adenosquamous, carcinoma cuniculatum	
Non-keratinising squamous cell carcinoma	8072/3
NUT carcinoma	8023/3
SWI/SNF complex-deficient sinonasal carcinoma	8044/3
Sinonasal lymphoepithelial carcinoma	8082/3
Sinonasal undifferentiated carcinoma	8020/3
Teratocarcinosarcoma	9081/3
HPV-related multiphenotypic sinonasal carcinoma	8483/3
<b>Adenocarcinoma</b>	
Intestinal-type adenocarcinoma	8144/3
Non-intestinal-type adenocarcinoma	8140/3
<b>Neuroendocrine neoplasms</b>	
Small cell neuroendocrine carcinoma	8041/3
Large cell neuroendocrine carcinoma	8013/3
Carcinoma mixed with small cell neuroendocrine carcinoma <sup>b</sup>	8045/3
Carcinoma mixed with large cell neuroendocrine carcinoma <sup>b</sup>	8013/3

<sup>a</sup>These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).<sup>26</sup> Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site: and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries. Subtype labels are indented.

<sup>b</sup>This terminology is synonymous with the ICD-O terminology of combined small/large cell neuroendocrine carcinomas.

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## Note 8 – Histological tumour grade (Core)

The applicability of tumour grading in the sinonasal tract is dependent on the histologic type (see Table 2). Most newly-described entities have no established grading scheme, but rather are known to have inherent biologic behaviour (e.g., NUT carcinoma is very aggressive, while human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma is relatively indolent).<sup>27,28</sup>

Still, several grading systems for each tumour type are available, with differing merits, and as such, recording which system has been applied is more clinically meaningfully (use ‘specify’ to state the system used), with the ICCR deferring to the WHO Classification current edition for grading guidance and preference.<sup>3</sup>



**Table 2: Applicable grading schemes for sinonasal tumour types.**

Histologic tumour type	Grading scheme
Keratinising squamous cell carcinoma	Well-, moderately-, or poorly-differentiated
Non-keratinising squamous cell carcinoma	Not applicable
NUT carcinoma	Not applicable
SWI/SNF complex-deficient sinonasal carcinoma	Not applicable
Sinonasal lymphoepithelial carcinoma	Not applicable
Sinonasal undifferentiated carcinoma	Not applicable
Neuroendocrine carcinoma	High grade
Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma	Not applicable
Intestinal-type sinonasal adenocarcinoma	Emerging data to support well-, moderately-, or poorly-differentiated scheme. <sup>29</sup>
Non-intestinal type sinonasal adenocarcinoma	Low grade or high grade
Salivary-type adenocarcinoma	See ICCR Carcinoma of major salivary glands dataset. <sup>25</sup>
Teratocarcinosarcoma	Not applicable

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## Note 9 – Extent of invasion (Core)

Bone and/or cartilage invasion is a frequent finding in sinonasal carcinomas. Both bone erosion and destruction have to be reported as part of the definition of the primary tumour in the TNM staging system.<sup>17,18</sup> Soft tissue infiltration and skull base involvement are incorporated into the staging.

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## Note 10 – Lymphovascular invasion (Core)

Lymphovascular invasion consists in the presence of neoplastic cells within an endothelial-lined space, either lymphatic or venous, and should be distinguished from retraction artefact. Immunohistochemical staining for an endothelial marker may help in this distinction.

Lymphovascular invasion is reported in up to 60% of sinonasal SSCs, but its clinical significance at this anatomic site remains to be determined.<sup>30</sup>

Cases that are still equivocal after taking additional steps may be reported as ‘indeterminate’ for lymphovascular invasion, but this designation should be sparingly used and it is useful to provide the reason in a comment in the report.

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## Note 11 – Perineural invasion (Core)

The frequency of perineural invasion in sinonasal carcinomas is lower than other head and neck sites, and varies according to the histologic subtype, being most frequent in adenoid cystic carcinoma, sinonasal undifferentiated carcinoma and SSC.<sup>30,31</sup> In sinonasal carcinomas, perineural invasion is associated with a high rate of positive margins, with variable results with respect to outcome.<sup>30,32</sup>

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## Note 12 – Margin status (Core)

As endoscopic procedures are now the predominant sinonasal tumour resection, margins are most often sent as numerous separate, fragmented specimens. Therefore, margins can usually only be reported as positive or negative, with distance to margin being impossible to determine. The significance of positive margins has been historically extrapolated from studies on oral cavity tumours,<sup>33-35</sup> but there is increasing evidence to support a worse outcome for sinonasal tumours as well.<sup>32,36-39</sup>

Surface dysplasia and carcinoma in situ are exceedingly rare in sinonasal carcinomas, but secondary surface spread from an invasive carcinoma can be seen.<sup>28,40</sup> For the purposes of this dataset, a margin with intraepithelial carcinoma should be regarded as positive for invasive carcinoma.

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## Note 13 – Precursor lesions (Core)

It is well established that sinonasal papillomas (especially the inverted and oncocytic subtypes) may give rise to sinonasal carcinomas, most often SSCs but rarely other types.<sup>41,42</sup> Surface dysplasia is rare in the sinonasal tract, but it is a characteristic precursor lesion in HPV-related multiphenotypic sinonasal carcinoma.<sup>28</sup> It has been suggested that some sinonasal non-salivary adenocarcinomas may arise from respiratory epithelial adenomatoid hamartoma or seromucinous hamartoma, but the precursor role of these lesions is unresolved.

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## Note 14 – Ancillary studies (Core and Non-core)

While keratinising SSC – the most common sinonasal malignancy – can be diagnosed by routine microscopy, ancillary techniques are becoming increasingly necessary to diagnose many sinonasal tumours (see Table 3). If the specific technique is not performed, then a note to that effect should be entered, along with the most likely candidate category (i.e., if NUT immunohistochemistry is not available, state non-keratinising SCC, and suggest it may be in this category).

While parts of this element are deemed core, consideration should be given to temporarily downgrading these to non-core until resources allow.

**Table 3: Core and non-core ancillary techniques for each sinonasal tumour type.**

Histologic tumour type	Ancillary techniques
Keratinising squamous cell carcinoma	Not needed in most cases (non-core).
Non-keratinising squamous cell carcinoma	Diffuse expression of squamous markers (e.g., p40, CK5/6) required (core). Negative CD99 is useful to exclude adamantinoma-like Ewing sarcoma, and negative NUT to exclude NUT carcinoma (non-core). Many are human papillomavirus (HPV)-related, but HPV testing is not currently required (non-core).
NUT carcinoma	Demonstration of <i>NUT</i> gene rearrangement or positivity with monoclonal antibody against NUT protein is required (core). <sup>43</sup>
SWI/SNF complex-deficient sinonasal carcinoma	Loss of expression of either SMARCB1 or SMARCA4 by immunohistochemistry is required (core). <sup>44,45</sup>
Sinonasal lymphoepithelial carcinoma	Usually positive for Epstein-Barr virus (EBV) by in situ hybridization. <sup>46</sup> Useful but not required (non-core).
Sinonasal undifferentiated carcinoma	Diagnosis of exclusion, so other similar-appearing entities (e.g., non-keratinising squamous cell carcinoma, NUT carcinoma, SWI/SNF complex-deficient sinonasal carcinomas) must be excluded (core). <sup>47</sup>
Neuroendocrine carcinoma	Positive staining with at least one specific neuroendocrine marker (synaptophysin, chromogranin, INSM1) and an epithelial marker required (core). Other tumours which express these markers must be excluded, e.g., olfactory neuroblastoma, teratocarcinosarcoma.
HPV-related multiphenotypic sinonasal carcinoma	HPV-specific testing (in situ hybridization or PCR) is required (core). Testing should include type 33 which is most common. <sup>48</sup>
Intestinal-type sinonasal adenocarcinoma	Immunostaining with CDX2 and CK20 is useful but not required (non-core). <sup>49</sup>
Non-intestinal type sinonasal adenocarcinoma	Often positive for SOX10, S100, and DOG1, with a subset showing nuclear beta-catenin expression, but not required for diagnosis (non-core). <sup>50,51</sup>
Salivary-type adenocarcinoma	See ICCR Carcinoma of major salivary glands dataset. <sup>25</sup>
Teratocarcinosarcoma	SMARCA4 is often completely or partially lost and beta-catenin staining is frequently nuclear. Useful in a limited sample, but not required to diagnose (non-core). <sup>52</sup>

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## Note 15 – Pathological staging (Core)

By Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) convention,<sup>17,18</sup> the designation ‘T’ refers to a primary tumour that has not been previously treated. The symbol ‘p’ refers to the pathologic classification of the stage, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumour 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. There is no pathologic M0 category as this designation requires clinical evaluation and imaging. Clinical classification (cTNM) is usually carried out by the evaluating clinician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathological staging is usually performed after surgical resection of the primary tumour and depends on 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 even though total removal of the primary cancer was not performed.

### 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 categorises the extent of tumour actually present at the time of that examination. The ‘y’ categorisation 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.

For the pN classification of regional lymph nodes, see ICCR Nodal excisions and neck dissection specimens dataset.<sup>2</sup>

Reporting of pathological staging categories (pT,pN,pM) is based on the evidence available to the pathologist at the time of reporting. As indicated in UICC TNM8 and AJCC TNM8,<sup>17,18</sup> the final stage grouping of a patient's tumour is based on a combination of pathological staging and other clinical and imaging information.

Pathological staging should not be reported if the submitted specimen is insufficient for definitive staging, especially with biopsy samples (core needle, incisional or excisional). Staging is based on the submitted resection, and even if there is grossly residual disease or there is tumour at the margin, pT staging should only be reported on findings in the resection specimen and/or at operation.<sup>17,18</sup>

The reference document TNM Supplement: A commentary on uniform use, 5<sup>th</sup> Edition (C Wittekind et al. editors) may be of assistance when staging.<sup>53</sup>

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## References

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