**Carcinomas of the Nasal Cavity and Paranasal Sinuses Histopathology Reporting Guide**

**Elements in black text are CORE Elements in grey text are NON-CORE o indicates single select values □ indicates multi-select values**

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| Definition of 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 evidence1). 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.  **Reference**  1 Merlin T, Weston A and Tooher R (2009). Extending an evidence hierarchy to include topics other than treatment: revising the Australian 'levels of evidence'. *BMC Med Res Methodol* 9:34. |
| Definition of 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 |
| Scope of this dataset | 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.1  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, 5th edition, 2024.2  **References**  1 International Collaboration on Cancer Reporting (2024). *Nodal Excisions and Neck Dissection Specimens for Head & Neck Tumours Histopathology Reporting Guide. 2nd edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/head-neck/nodal-excisions/ (Accessed 31st July 2024).  2 WHO Classification of Tumours Editorial Board (2024). *Head and Neck Tumours, WHO Classification of Tumours, 5th Edition, Volume 10.* IARC Press, Lyon. |

| **Core/**  **Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| --- | --- | --- | --- | --- |
| Core and Non-core | CLINICAL INFORMATION | * 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* | 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.1-4  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.  **References**  1 Nibu K, Sugasawa M, Asai M, Ichimura K, Mochiki M, Terahara A, Kawahara N and Asato H (2002). Results of multimodality therapy for squamous cell carcinoma of maxillary sinus. *Cancer* 94(5):1476-1482.  2 Samant S, Robbins KT, Vang M, Wan J and Robertson J (2004). Intra-arterial cisplatin and concomitant radiation therapy followed by surgery for advanced paranasal sinus cancer. *Arch Otolaryngol Head Neck Surg* 130(8):948-955.  3 Madison Michael L, 2nd, Sorenson JM, Samant S and Robertson JH (2005). The treatment of advanced sinonasal malignancies with pre-operative intra-arterial cisplatin and concurrent radiation. *J Neurooncol* 72(1):67-75.  4 Licitra L, Suardi S, Bossi P, Locati LD, Mariani L, Quattrone P, Lo Vullo S, Oggionni M, Olmi P, Cantu G, Pierotti MA and Pilotti S (2004). Prediction of TP53 status for primary cisplatin, fluorouracil, and leucovorin chemotherapy in ethmoid sinus intestinal-type adenocarcinoma. *J Clin Oncol* 22(24):4901-4906. |  |
| Core | OPERATIVE PROCEDURE | * Not specified * Biopsy (excisional, incisional, core needle), *specify* * Resection * Open * Endoscopic * Combined * En bloc * Piecemeal * Neck (lymph node) dissection, a *specify* * Other, *specify* | 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.1-3 This results in a wide range of surgical specimens submitted for histopathological analysis.  **References**  1 Meccariello G, Deganello A, Choussy O, Gallo O, Vitali D, De Raucourt D and Georgalas C (2016). Endoscopic nasal versus open approach for the management of sinonasal adenocarcinoma: A pooled-analysis of 1826 patients. *Head Neck* 38 Suppl 1:E2267-2274.  2 Roxbury CR, Ishii M, Richmon JD, Blitz AM, Reh DD and Gallia GL (2016). Endonasal Endoscopic Surgery in the Management of Sinonasal and Anterior Skull Base Malignancies. *Head Neck Pathol* 10(1):13-22.  3 Llorente JL, Lopez F, Suarez C and Hermsen MA (2014). Sinonasal carcinoma: clinical, pathological, genetic and therapeutic advances. *Nat Rev Clin Oncol* 11(8):460-472. | a If a neck (lymph node) dissection is submitted, then a separate dataset is used to record the information. |
| Core | SPECIMEN(S) SUBMITTED | * Not specified * Nasal cavity, *specify* * Paranasal sinus(es), *specify* * Orbit, *specify* * Neck (lymph node) dissection,a *specify* * Other, *specify* | 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.1  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’.  **Reference**  1 Slootweg PJ (2005). Complex head and neck specimens and neck dissections. How to handle them. *J Clin Pathol* 58(3):243-248. | a If a neck (lymph node) dissection is submitted, then a separate dataset is used to record the information. |
| Core | TUMOUR SITE | * Not specified * Nasal cavity * Septum * Floor * Lateral wall * Vestibule * Paranasal sinus(es), maxillary * Paranasal sinus(es), ethmoid * Cribriform plate * Paranasal sinus(es), frontal * Paranasal sinus(es), sphenoid * Orbit * Cranial cavity * Other, *specify* | 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 of pituitary origin.1-5  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.6,7 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.1,5,8,9 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.6,7 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.10-13  It is recognised that many carcinomas affect more than one sinonasal anatomic sub-site. In this case, every affected site should be selected.  **References**  1 Ansa B, Goodman M, Ward K, Kono SA, Owonikoko TK, Higgins K, Beitler JJ, Grist W, Wadsworth T, El-Deiry M, Chen AY, Khuri FR, Shin DM and Saba NF (2013). Paranasal sinus squamous cell carcinoma incidence and survival based on Surveillance, Epidemiology, and End Results data, 1973 to 2009. *Cancer* 119(14):2602-2610.  2 Robin PE, Powell DJ and Stansbie JM (1979). Carcinoma of the nasal cavity and paranasal sinuses: incidence and presentation of different histological types. *Clin Otolaryngol Allied Sci* 4(6):431-456.  3 Sanghvi S, Khan MN, Patel NR, Yeldandi S, Baredes S and Eloy JA (2014). Epidemiology of sinonasal squamous cell carcinoma: a comprehensive analysis of 4994 patients. *Laryngoscope* 124(1):76-83.  4 Takahashi Y, Bell D, Agarwal G, Roberts D, Xie TX, El-Naggar A, Myers JN and Hanna EY (2014). Comprehensive assessment of prognostic markers for sinonasal squamous cell carcinoma. *Head Neck* 36(8):1094-1102.  5 Turner JH and Reh DD (2012). Incidence and survival in patients with sinonasal cancer: a historical analysis of population-based data. *Head Neck* 34(6):877-885.  6 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  7 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.  8 Dulguerov P, Jacobsen MS, Allal AS, Lehmann W and Calcaterra T (2001). Nasal and paranasal sinus carcinoma: are we making progress? A series of 220 patients and a systematic review. *Cancer* 92(12):3012-3029.  9 Thorup C, Sebbesen L, Dano H, Leetmaa M, Andersen M, Buchwald C, Kristensen CA, Bentzen J, Godballe C, Johansen J and Grau C (2010). Carcinoma of the nasal cavity and paranasal sinuses in Denmark 1995-2004. *Acta Oncol* 49(3):389-394.  10 Klintenberg C, Olofsson J, Hellquist H and Sokjer H (1984). Adenocarcinoma of the ethmoid sinuses. A review of 28 cases with special reference to wood dust exposure. *Cancer* 54(3):482-488.  11 Mitchell EH, Diaz A, Yilmaz T, Roberts D, Levine N, DeMonte F, Hanna EY and Kupferman ME (2012). Multimodality treatment for sinonasal neuroendocrine carcinoma. *Head Neck* 34(10):1372-1376.  12 Smith SR, Som P, Fahmy A, Lawson W, Sacks S and Brandwein M (2000). A clinicopathological study of sinonasal neuroendocrine carcinoma and sinonasal undifferentiated carcinoma. *Laryngoscope* 110(10 Pt 1):1617-1622.  13 Moreno MA, Roberts DB, Kupferman ME, DeMonte F, El-Naggar AK, Williams M, Rosenthal DS and Hanna EY (2010). Mucosal melanoma of the nose and paranasal sinuses, a contemporary experience from the M. D. Anderson Cancer Center. *Cancer* 116(9):2215-2223. |  |
| Core | TUMOUR LATERALITY | * Not specified * Left * Right * Midline |  |  |
| Non-core | TUMOUR DIMENSIONS | Maximum tumour dimension (largest tumour) (pathology and/or imaging determination)  \_\_\_ mm  Additional dimensions  (largest tumour)  \_\_\_ mm x \_\_\_ mm | 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. |  |
| Non-core | BLOCK IDENTIFICATION KEY | List overleaf or separately with an indication of the nature and origin of all tissue blocks. | 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. |  |
| Core | HISTOLOGICAL TUMOUR TYPE | (Select all that apply)   * 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,b *specify type* * Neuroendocrine neoplasm * Small cell neuroendocrine carcinoma * Large cell neuroendocrine carcinoma * Carcinoma mixed with neuroendocrine carcinoma * Other, *specify* | All sinonasal tumours should be classified based on the most recent edition of the World Health Organization (WHO) Classification of Head and Neck Tumours, 5th edition, 2024 (Table 1).1 The list of histologic types discussed in the chapter on sinonasal tumours in the 5th 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 International Collaboration on Cancer Reporting (ICCR) Carcinomas of the major salivary glands dataset for guidance on histological typing.2 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 **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 (See end of the document for Tables)**  **References**  1 WHO Classification of Tumours Editorial Board (2024). *Head and Neck Tumours, WHO Classification of Tumours, 5th Edition, Volume 10.* IARC Press, Lyon.  2 International Collaboration on Cancer Reporting (2024). *Carcinomas of the major salivary glands Histopathology Reporting Guide. 2nd edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/head-neck/salivary-glands/ (Accessed 31st July 2024).  3 Fritz A, Percy C, Jack A,  Shanmugaratnam K, Sobin L, Parkin DM  and Whelan S (eds) (2020). *International Classification of Diseases for Oncology, Third edition, Second revision ICD-O-3.2*. Available from: http://www.iacr.com.fr/index.php?option=com\_content&view=category&layout=blog&id=100&Itemid=577 (Accessed 16th March 2024). | Value list based on the WHO  Classification of Head and Neck Tumours (2024).  Note that permission to publish the WHO Classification of Tumours may be needed in your implementation. It is advisable to check with the International Agency for Research on Cancer (IARC).  b For histological type of salivary gland-type carcinomas, refer to the  Carcinomas of the major salivary glands dataset. |
| Core | HISTOLOGICAL TUMOUR GRADEc | * 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* | 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).1,2  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.3  **Table 2 (See end of the document for Tables)**  **References**  1 Chau NG, Ma C, Danga K, Al-Sayegh H, Nardi V, Barrette R, Lathan CS, DuBois SG, Haddad RI, Shapiro GI, Sallan SE, Dhar A, Nelson JJ and French CA (2020). An Anatomical Site and Genetic-Based Prognostic Model for Patients With Nuclear Protein in Testis (NUT) Midline Carcinoma: Analysis of 124 Patients. *JNCI Cancer Spectr* 4(2):pkz094.  2 Bishop JA, Andreasen S, Hang JF, Bullock MJ, Chen TY, Franchi A, Garcia JJ, Gnepp DR, Gomez-Fernandez CR, Ihrler S, Kuo YJ, Lewis JS, Jr., Magliocca KR, Pambuccian S, Sandison A, Uro-Coste E, Stelow E, Kiss K and Westra WH (2017). HPV-related Multiphenotypic Sinonasal Carcinoma: An Expanded Series of 49 Cases of the Tumor Formerly Known as HPV-related Carcinoma With Adenoid Cystic Carcinoma-like Features. *Am J Surg Pathol* 41(12):1690-1701.  3 WHO Classification of Tumours Editorial Board (2024). *Head and Neck Tumours, WHO Classification of Tumours, 5th Edition, Volume 10.* IARC Press, Lyon.  4 de Gabory L, Waubant A, Verillaud B, Michel J, Malard O, Rumeau C, Jankowski R, Moya-Plana A, Vergez S, Favier V, Mortuaire G, Righini C, Patron V, Thariat J, Dupin C, Coelho J and Bénard A (2023). Multicenter study to assess surgical treatments of 452 sinonasal intestinal-type adenocarcinomas: A REFCOR study. *Eur J Surg Oncol* 49(1):39-46.  5 International Collaboration on Cancer Reporting (2024). *Carcinomas of the major salivary glands Histopathology Reporting Guide. 2nd edition*. Available from: https://www.iccr-cancer.org/datasets/published-datasets/head-neck/salivary-glands/ (Accessed 31st July 2024). | Not applicable to all tumours.  c 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. |
| Core | EXTENT OF INVASION | * Not identified * Present (select all that apply)   Clinical observation Histologic    and/or imaging     * 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* | 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.1,2 Soft tissue infiltration and skull base involvement are incorporated into the staging.  **References**  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *Union for International Cancer Control.* *TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York. |  |
| Core | LYMPHOVASCULAR INVASION | * Not identified * Present * Indeterminate, *specify reason* | 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 squamous cell carcinomas, but its clinical significance at this anatomic site remains to be determined.1  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.  **Reference**  1 Gil Z, Carlson DL, Gupta A, Lee N, Hoppe B, Shah JP and Kraus DH (2009). Patterns and incidence of neural invasion in patients with cancers of the paranasal sinuses. *Arch Otolaryngol Head Neck Surg* 135(2):173-179. |  |
| Core | PERINEURAL INVASION | * Not identified * Present * Indeterminate, *specify reason* | 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 squamous cell carcinoma.1,2 In sinonasal carcinomas, perineural invasion is associated with a high rate of positive margins, with variable results with respect to outcome.1,3  **References**  1 Gil Z, Carlson DL, Gupta A, Lee N, Hoppe B, Shah JP and Kraus DH (2009). Patterns and incidence of neural invasion in patients with cancers of the paranasal sinuses. *Arch Otolaryngol Head Neck Surg* 135(2):173-179.  2 Hanna E, Vural E, Prokopakis E, Carrau R, Snyderman C and Weissman J (2007). The sensitivity and specificity of high-resolution imaging in evaluating perineural spread of adenoid cystic carcinoma to the skull base. *Arch Otolaryngol Head Neck Surg* 133(6):541-545.  3 Sacks PL, Alvarado R, Sacks R, Kalish L, Campbell R and Harvey R (2022). Prognostic factors and outcomes in minimal access resections of skull base and sinonasal epithelial malignancy. *ANZ J Surg* 92(12):3253-3258. |  |
| Core | MARGIN STATUS | * Not involved by invasive carcinoma     Specify closest margin(s), if  possible   * Involved by invasive carcinoma   Specify margin(s), if possible   * Cannot be assessed, *specify* | 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,1-3 but there is increasing evidence to support a worse outcome for sinonasal tumours as well.4-8  Surface dysplasia and carcinoma in situ are exceedingly rare in sinonasal carcinomas, but secondary surface spread from an invasive carcinoma can be seen.9,10 For the purposes of this dataset, a margin with intraepithelial carcinoma should be regarded as positive for invasive carcinoma.  **References**  1 Hinni ML, Ferlito A, Brandwein-Gensler MS, Takes RP, Silver CE, Westra WH, Seethala RR, Rodrigo JP, Corry J, Bradford CR, Hunt JL, Strojan P, Devaney KO, Gnepp DR, Hartl DM, Kowalski LP, Rinaldo A and Barnes L (2013). Surgical margins in head and neck cancer: a contemporary review. *Head Neck* 35(9):1362-1370.  2 Ch'ng S, Corbett-Burns S, Stanton N, Gao K, Shannon K, Clifford A, Gupta R and Clark JR (2013). Close margin alone does not warrant postoperative adjuvant radiotherapy in oral squamous cell carcinoma. *Cancer* 119(13):2427-2437.  3 Sutton DN, Brown JS, Rogers SN, Vaughan ED and Woolgar JA (2003). The prognostic implications of the surgical margin in oral squamous cell carcinoma. *Int J Oral Maxillofac Surg* 32(1):30-34.  4 Sacks PL, Alvarado R, Sacks R, Kalish L, Campbell R and Harvey R (2022). Prognostic factors and outcomes in minimal access resections of skull base and sinonasal epithelial malignancy. *ANZ J Surg* 92(12):3253-3258.  5 Ferrari M, Mattavelli D, Tomasoni M, Raffetti E, Bossi P, Schreiber A, Orlandi E, Taboni S, Rampinelli V, Gualtieri T, Turri-Zanoni M, Battaglia P, Arosio AD, Bignami M, Tartaro T, Molteni M, Bertazzoni G, Fiaux-Camous D, Jourdaine C, Verillaud B, Eu D, Nair D, Moiyadi A, Shetty P, Ghosh-Laskar S, Budrukkar A, Magrini SM, Guillerm S, Faivre S, Piazza C, Gilbert RW, Irish JC, de Almeida JR, Pai P, Herman P, Castelnuovo P and Nicolai P (2022). The MUSES∗: a prognostic study on 1360 patients with sinonasal cancer undergoing endoscopic surgery-based treatment: ∗MUlti-institutional collaborative Study on Endoscopically treated Sinonasal cancers. *Eur J Cancer* 171:161-182.  6 Arosio AD, Bernasconi DP, Valsecchi MG, Pacifico C, Battaglia P, Bignami M, Ferrari M, Mattavelli D, Rampinelli V, Tomasoni M, Schreiber A, Gualtieri T, Piazza C, Magrini SM, Tartaro T, Molteni M, Lambertoni A, Sileo G, Bossi P, Orlandi E, Bertazzoni G, Fiaux-Camous D, Jourdaine C, Verillaud B, Herman P, Nicolai P, Castelnuovo P and Turri-Zanoni M (2022). Patterns of recurrences in sinonasal cancers undergoing an endoscopic surgery-based treatment: Results of the MUSES\* on 940 patients: \*MUlti-institutional collaborative Study on Endoscopically treated Sinonasal cancers. *Oral Oncol* 134:106123.  7 Torabi SJ, Spock T, Cardoso B, Chao J, Morse E, Manes RP and Judson BL (2020). Margins in Sinonasal Squamous Cell Carcinoma: Predictors, Outcomes, and the Endoscopic Approach. *Laryngoscope* 130(6):E388-e396.  8 Jafari A, Shen SA, Qualliotine JR, Orosco RK, Califano JA and DeConde AS (2019). Impact of margin status on survival after surgery for sinonasal squamous cell carcinoma. *Int Forum Allergy Rhinol* 9(10):1205-1211.  9 Shah AA, Jain D, Ababneh E, Agaimy A, Hoschar AP, Griffith CC, Magliocca KR, Wenig BM, Rooper LM and Bishop JA (2020). SMARCB1 (INI-1)-Deficient Adenocarcinoma of the Sinonasal Tract: A Potentially Under-Recognized form of Sinonasal Adenocarcinoma with Occasional Yolk Sac Tumor-Like Features. *Head Neck Pathol* 14(2):465-472.  10 Bishop JA, Andreasen S, Hang JF, Bullock MJ, Chen TY, Franchi A, Garcia JJ, Gnepp DR, Gomez-Fernandez CR, Ihrler S, Kuo YJ, Lewis JS, Jr., Magliocca KR, Pambuccian S, Sandison A, Uro-Coste E, Stelow E, Kiss K and Westra WH (2017). HPV-related Multiphenotypic Sinonasal Carcinoma: An Expanded Series of 49 Cases of the Tumor Formerly Known as HPV-related Carcinoma With Adenoid Cystic Carcinoma-like Features. *Am J Surg Pathol* 41(12):1690-1701. |  |
| Core | PRECURSOR LESIONS | * Not applicable * Not present * Present (e.g., sinonasal papilloma (type), surface dysplasia), *specify* | It is well established that sinonasal papillomas (especially the inverted and oncocytic subtypes) may give rise to sinonasal carcinomas, most often squamous cell carcinomas but rarely other types.1,2 Surface dysplasia is rare in the sinonasal tract, but it is a characteristic precursor lesion in human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma.3 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.    **References**  1 Nudell J, Chiosea S and Thompson LD (2014). Carcinoma ex-Schneiderian papilloma (malignant transformation): a clinicopathologic and immunophenotypic study of 20 cases combined with a comprehensive review of the literature. *Head Neck Pathol* 8(3):269-286.  2 Maisch S, Mueller SK, Traxdorf M, Weyerer V, Stoehr R, Iro H, Hartmann A and Agaimy A (2020). Sinonasal papillomas: A single centre experience on 137 cases with emphasis on malignant transformation and EGFR/KRAS status in "carcinoma ex papilloma". *Ann Diagn Pathol* 46:151504.  3 Bishop JA, Andreasen S, Hang JF, Bullock MJ, Chen TY, Franchi A, Garcia JJ, Gnepp DR, Gomez-Fernandez CR, Ihrler S, Kuo YJ, Lewis JS, Jr., Magliocca KR, Pambuccian S, Sandison A, Uro-Coste E, Stelow E, Kiss K and Westra WH (2017). HPV-related Multiphenotypic Sinonasal Carcinoma: An Expanded Series of 49 Cases of the Tumor Formerly Known as HPV-related Carcinoma With Adenoid Cystic Carcinoma-like Features. *Am J Surg Pathol* 41(12):1690-1701. |  |
| Core and Non-core | ANCILLARY STUDIES | * Not performed * Performed   If performed, specify (select all that apply)  **Non-keratinising squamous cell carcinoma**   * Positive * Pancytokeratin * p40 * p63 * CK5/6 * Negative * CD99 * NKX2.2 * NUT * INI1 * Retained * Deficient * BRG1 * Retained * Deficient   **NUT carcinoma**   * Positive * NUT immunohistochemistry * NUTM1 gene rearrangement, *specify technique*   **SWI/SNF complex-deficient sinonasal carcinoma**   * INI1 * Retained * Deficient * BRG1 * Retained * Deficient   **Sinonasal undifferentiated carcinoma**   * Positive * Pancytokeratin * IDH1/2 * CK7 * Negative * p40/p63 * CK5/6 * CD99 * NKX2.2 * NUT * 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 * Chromogranin * Synaptophysin * INSM1 * Ki-67 proliferation index \_\_\_% * Rb * Retained * Deficient   **Keratinising squamous cell**  **carcinoma**   * Positive * Pancytokeratin * p40 * p63 * CK5/6   **Sinonasal lymphoepithelial**  **carcinoma**   * Positive * Pancytokeratin * P16 * EBER in situ hybridization   **Teratocarcinosarcoma**   * Positive * Nuclear ß-catenin * BRG4 (SMARCA4) * Retained * Deficient   **Intestinal-type sinonasal**  **adenocarcinoma**   * Positive * CDX2 * CK20 * CK7 * SATB2 * Villin   **Non-intestinal-type sinonasal**  **adenocarcinoma**   * Positive * CK7 * SOX10 * DOG1 * S100 protein * Nuclear ß-catenin * Negative * CK20 * CDX2   **Other ancillary studies,** r*ecord*  *test(s), methodology and results*  **Representative blocks for ancillary studies**, *specify those blocks best representing tumour and/or normal tissue for further study* | 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 (See end of the document for Tables)**  **References**  1 Haack H, Johnson LA, Fry CJ, Crosby K, Polakiewicz RD, Stelow EB, Hong SM, Schwartz BE, Cameron MJ, Rubin MA, Chang MC, Aster JC and French CA (2009). Diagnosis of NUT midline carcinoma using a NUT-specific monoclonal antibody. *Am J Surg Pathol* 33(7):984-991.  2 Agaimy A, Hartmann A, Antonescu CR, Chiosea SI, El-Mofty SK, Geddert H, Iro H, Lewis JS, Jr., Märkl B, Mills SE, Riener MO, Robertson T, Sandison A, Semrau S, Simpson RH, Stelow E, Westra WH and Bishop JA (2017). 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| Core | PATHOLOGICAL STAGING  (UICC TNM 8**th** edition)d | **TNM Descriptors** (only if applicable) (select all that apply)   * m - multiple primary tumours * r - recurrent * y - during or following multimodality therapy   **Primary tumour (pT)e**   * TXf 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 | By Union for International Cancer Control (UICC)/American Joint Committee on Cancer (AJCC) convention,1,2 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.3  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 TNM8,1,2 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.1,2  The reference document TNM Supplement: A commentary on uniform use, 5th Edition (C Wittekind et al. editors) may be of assistance when staging.4  **References**  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). *Union for International Cancer Control.* *TNM Classification of Malignant Tumours, 8th Edition*, Wiley, USA.  2 Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD, Gaspar LE, Schilsky RL, Balch CM, Winchester DP, Asare EA, Madera M, Gress DM and Meyer LR (eds) (2017). *AJCC Cancer Staging Manual. 8th ed.*, Springer, New York.  3 International Collaboration on Cancer Reporting (2024). *Nodal Excisions and Neck Dissection Specimens for Head & Neck Tumours Histopathology Reporting Guide. 2nd edition*. 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**Tables**

## **Table 1: World Health Organization classification of tumours of the nasal cavity, paranasal sinuses and skull base.1**

| **Descriptor** | **ICD-O codesa** |
| --- | --- |
| **Carcinomas** |  |
| 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 |
| Adenocarcinoma |  |
| Intestinal-type adenocarcinoma | 8144/3 |
| Non-intestinal-type adenocarcinoma | 8140/3 |
| Neuroendocrine neoplasms |  |
| Small cell neuroendocrine carcinoma | 8041/3 |
| Large cell neuroendocrine carcinoma | 8013/3 |
| Carcinoma mixed with small cell neuroendocrine carcinomab | 8045/3 |
| Carcinoma mixed with large cell neuroendocrine carcinomab | 8013/3 |

a These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-0-3.2).3 Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour: /2 for carcinoma in situ and grade Ill 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.

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

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**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.4 |
| Non-intestinal type sinonasal adenocarcinoma | Low grade or high grade |
| Salivary-type adenocarcinoma | See ICCR Carcinoma of major salivary glands dataset.5 |
| Teratocarcinosarcoma | Not applicable |

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**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 not currently required (non-core). |
| NUT carcinoma | Demonstration of *NUT* gene rearrangement or positivity with monoclonal antibody against NUT protein is required (core).1 |
| SWI/SNF complex-deficient sinonasal carcinoma | Loss of expression of either SMARCB1 or SMARCA4 by immunohistochemistry is required (core).2,3 |
| Sinonasal lymphoepithelial carcinoma | Usually positive for Epstein-Barr virus (EBV) by in situ hybridization.4 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).5 |
| 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.6 |
| Intestinal-type sinonasal adenocarcinoma | Immunostaining with CDX2 and CK20 is useful but not required (non-core).7 |
| 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).8,9 |
| Salivary-type adenocarcinoma | See ICCR Carcinoma of major salivary glands dataset.10 |
| 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).11 |

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