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Mucosal Melanomas of the Head and Neck Histopathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

SCOPE OF THIS DATASET

OPERATIVE PROCEDURE (select all that apply)

- ○ Not specified
- ☐ Biopsy (excisional, incisional), *specify*
- ☐ Resection, *specify (e.g. maxillectomy, hemiglossectomy, partial laryngectomy, etc.)*
- ☐ Neck (lymph node) dissection*, *specify*
- ☐ Other, *specify*

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

SPECIMENS SUBMITTED (Note 1)

- ○ Not specified
- ☐ Anatomic site, *specify (may be multiple separate sites, but excluding lymph node dissection as that is a separate form)*

TUMOUR SITE (select all that apply) (Note 2)

- ○ Cannot be assessed
- ☐ Sinonasal, *specify subsite(s)*
  - ☐ Left ☐ Right
  - ☐ Midline ○ Laterality not specified
  - Subsite(s)
- ☐ Oral cavity, *specify subsite(s)*
  - ☐ Left ☐ Right
  - ☐ Midline ○ Laterality not specified
  - Subsite(s)
- ☐ Larynx, *specify subsite(s)*
  - ☐ Left ☐ Right
  - ☐ Midline ○ Laterality not specified
  - Subsite(s)
- ☐ Nasopharynx, *specify subsites(s)*
  - ☐ Left ☐ Right
  - ☐ Midline ○ Laterality not specified
  - Subsite(s)
- ☐ Other, *specify site/subsite(s)*
  - ☐ Left ☐ Right
  - ☐ Midline ○ Laterality not specified
  - Site/subsite(s)

TUMOUR FOCALITY

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

TUMOUR DIMENSIONS (Note 3)

Maximum tumour dimension (largest focus in a single specimen)

mm

Additional dimensions (largest tumour)

mm x mm

- ○ Cannot be assessed, *specify*

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HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 4)

(Value list from the World Health Organization Classification of Head and Neck Tumours (2017))

- ☐ Mucosal melanoma
- ☐ Melanoma (uncertain origin), *specify/comment*

Histologic subtypes

- ☐ Balloon cell melanoma
- ☐ Mixed epithelioid and spindle cell melanoma
- ☐ Epithelioid cell melanoma
- ☐ Spindle cell melanoma
- ☐ Amelanotic melanoma
- ☐ Undifferentiated melanoma
- ☐ Other, *specify*
- ○ Cannot be assessed, *specify*

MARGIN STATUS (Note 5)

Invasive melanoma

- ○ Involved
  - Specify margin(s), if possible
- ○ Not involved
  - Distance of melanoma from closest margin ____ mm
  - ○ Distance not assessable
  - Specify closest margin, if possible

Melanoma in situ

- ○ Involved
  - Specify margin(s), if possible
- ○ Not involved
  - Distance of melanoma from closest margin ____ mm
  - ○ Distance not assessable
  - Specify closest margin, if possible

- ○ Cannot be assessed, *specify*

COEXISTENT PATHOLOGY (select all that apply) (Note 6)

- ○ None identified
- ☐ Melanoma in situ/pagetoid spread
- ☐ Melanosis
- ☐ Other, *specify*

ANCILLARY STUDIES (Note 7)

- ○ Not performed
- ○ Performed, *specify*

PATHOLOGICAL STAGING (UICC TNM 8th edition)## (Note 8)

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

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

Primary tumour (pT)**

- ○ TX Primary tumour cannot be assessed
- ○ T3 Tumour limited to the epithelium and/or submucosa (mucosal disease)
- ○ T4a Moderately advanced disease
  Tumour invades deep soft tissue, cartilage, bone, or overlying skin
- ○ T4b Very advanced disease
  Tumour invades any of the following: brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, or mediastinal structures

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

Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2017, Publisher Wiley-Blackwell.

Scope

The dataset has been developed for the reporting of resection and biopsy specimens of mucosal melanoma arising in the nasopharynx, oropharynx, larynx, hypopharynx, oral cavity, nasal cavity and paranasal sinuses. All other malignancies and tumour categories are dealt with in separate datasets, specifically cutaneous melanoma is separately reported.

Direct extension of a cutaneous primary into a mucosal site should be excluded, and would not be reported in this dataset (see above). Metastasis to a head and neck mucosal site is also excluded. If there are overlapping sites, clinical centering of the tumour should determine the dataset completed. If a primary tumour extends to involve the contralateral side, the tumour is still considered a unifocal tumour, but involving multiple, contiguous sites. If there are two topograpically distinct and separate tumours, they are considered multifocal, and in this setting a separate dataset should be completed for each tumour. In cases where there is uncertainty, one dataset should be completed, with multifocal tumours selected.

Neck dissections and nodal excisions are dealt with in a separate dataset, and this dataset should be used in conjunction, where applicable.

Note 1 – Specimens submitted (Core)

Reason/Evidentiary Support

The surgical approach for mucosal melanoma largely depends on the site of the primary tumour. In some locations such as gingiva, a single specimen may be received with/without additional separate margins. This may be a mucosal based resection or a composite resection with underlying tissues including bone. In the sinonasal cavity, while there may be a primary tumour specimen, numerous further specimens are received from contiguous anatomic sites in a 3-dimensional approach. The specimens submitted help to delineate the anatomic extent required for resection and may include bilateral tissues. Lymph node dissections are dealt with in a separate dataset.

Back

Note 2 – Tumour site (Core)

Reason/Evidentiary Support

Mucosal melanomas of the head and neck show specific sites of predilection, but in general are rare.

Nasal cavity: The majority of tumours are identified within the nasal cavity or septum, while other anatomic sites are rarely affected.[1,2]

Oral cavity: Most tumours are found on the palate or gingiva, although any site may be affected.[3-5]

Primary melanoma within nasopharynx, oropharynx, larynx and hypopharynx are exceedingly uncommon. However, nasopharyngeal primaries have an even worse prognosis than other head and neck sites.[1]

⬆ **Back**

Note 3 – Tumour dimensions (Core and Non-core)

Reason/Evidentiary Support

Unlike melanoma in cutaneous sites, tumour thickness (Breslow) and tumour level (Clark) are not clinically significant as a prognostic factor, nor are they easily determined due to the specimen type.[6] Overall tumour size (using 3 cm as a cut-off) is known to be associated with a worse prognosis,[1,7-9] but does not impact on T stage. The single largest tumour dimension in any one of the samples submitted should be entered, as trying to combine multiple smaller measurements from multiple different sites (especially if fragmented) does not yield clinically meaningful data.

⬆ **Back**

Note 4 – Histological tumour type (Core and Non-core)

Reason/Evidentiary Support

The inclusion of the specific histologic type or pattern of melanoma is primarily for differential diagnostic considerations, while the specific type does not impact patient outcome or management.[1,8] As mucosal melanomas are molecularly distinct from those of cutaneous origin occasional cases may require further molecular evaluation prior to definitively classifying as being of mucosal origin.

⬆ **Back**

Note 5 – Margin status (Non-core)

Reason/Evidentiary Support

In general, tumour margins are reported, but margin status is not an independent prognostic factor for head and neck mucosal melanomas. Further, melanoma in situ (if detected) may not be meaningful and thus reporting is encouraged but is not a core element.

⬆ **Back**

Note 6 – Coexistent pathology (Non-core)

Reason/Evidentiary Support

Melanosis is considered to be a potential precursor, although with conflicting data based on anatomic site and geographic distribution of the reported patients.[10-12] Pagetoid spread within the surface epithelium is often identical to melanoma in situ, without a meaningful separation between these entities at this time.

Back

Note 7 – Ancillary studies (Non-core)

Reason/Evidentiary Support

The diagnosis of melanoma is supported by the use of melanoma markers, including S100 protein, SOX10, HMB45, Melan A and tyrosinase, among others. Further, molecular studies can also be performed in selected cases, either for diagnostic purposes (helping to confirm the diagnosis), or for potential use in targeted therapies based on the results. Molecular findings in mucosal melanoma are different from cutaneous primaries, with *KIT* and *NRAS* mutations occurring more frequently than *BRAF* mutations in tumours of mucosal sites.[13-17]

Back

Note 8 – Pathological staging (Core)

Reason/Evidentiary Support

By American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) convention, the designation “T” refers to a primary tumour that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumour or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

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

TNM Descriptors

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

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

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

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

Additional Descriptors

<u>Residual Tumour (R)</u>

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

RX Presence of residual tumour cannot be assessed
R0 No residual tumour
R1 Microscopic residual tumour
R2 Macroscopic residual tumour

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

The 8th edition of the AJCC/UICC staging of head and neck cancers includes a separate chapter for mucosal melanomas.[18,19] Approximately two-thirds of mucosal melanomas arise in the sinonasal tract, one-quarter are found in the oral cavity and the remainder occur only sporadically in other mucosal sites of the head and neck.[20] Even small tumours behave aggressively with high rates of recurrence and death.[20] To reflect this aggressive behaviour, primary cancers limited to the mucosa are considered T3 lesions.

Advanced mucosal melanomas are classified as T4a and T4b. The anatomic extent criteria to define moderately advanced (T4a) and very advanced (T4b) disease are given above. The AJCC staging for mucosal melanomas does not provide for the histologic definition of a T3 lesion; as the majority of mucosal melanomas are invasive at presentation, mucosal based melanomas (T3 lesions) include

those lesions that involve either the epithelium and/or lamina propria of the involved site. Rare examples of in situ mucosal melanomas occur but in situ mucosal melanomas are excluded from staging, as they are extremely rare.[20]

Back

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