Sponsored by IMPSG International Melanoma Pathology Study Group

Merkel Cell Carcinoma Histopathology Reporting Guide

ICCR

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.

☐ 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 history of cancer, *specify*
- ☐ Other clinical information, *specify*

SPECIMEN(S) SUBMITTED (select all that apply) (Note 2)

- ☐ Skin
- ☐ Lymph node(s), *specify sentinel lymph node if known/ applicable*
- ☐ Other, *specify*

PROCEDURE (select all that apply) (Note 3)

- ◯ Not specified
- ☐ Excision (or resection)
- ☐ Biopsy (e.g., curettage, shave, punch, elliptical), *specify if possible*

TUMOUR SITE (Note 4)

◯ Not specified

◯ *Specify site*

If applicable also indicate

- ◯ Left
- ◯ Midline
- ◯ Right

MACROSCOPIC PRIMARY LESION DESCRIPTION (Note 5)

BLOCK IDENTIFICATION KEY (Note 6)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

TUMOUR DIMENSIONS (Note 7)

Maximum tumour diameter (clinical measurement) mm

Maximum tumour diameter (macroscopic measurement) mm

Maximum diameter of primary tumour (microscopic measurement) mm

◯ Indeterminate (e.g., no clinical information provided or submitted slide likely not representative)

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MERKEL CELL POLYOMAVIRUS (MCPyV) (Note 8)

- ◯ Results not known
- ◯ Results pending
- ◯ Testing for MCPyV not performed
- ◯ Testing for MCPyV performed, *specify method(s) and result(s)*

HISTOLOGICAL TUMOUR TYPE (Note 9)

- ◯ Merkel cell carcinoma (MCC)[a]
- ◯ MCC with morphological diversity,[b] *specify*

[a] *Pure or classic MCC, i.e., not admixed with another tumour type.*

[b] *Carcinoma with phenotypic heterogeneity that includes a neuroendocrine component. Most will show features of squamous cell carcinoma and neuroedocrine carcinoma.*

EXTENT OF INVASION (select all that apply) (Note 10)

- ◯ Cannot be assessed
- ◯ Invasion not identified (i.e., only in situ/intra-epithelial neoplastic proliferation)
- ☐ Tumour invades dermis
- ☐ Tumour invades subcutis
- ☐ Tumour invades deep fascia
- ☐ Tumour invades into skeletal muscle
- ☐ Tumour invades into bone
- ☐ Tumour invades cartilage
- ☐ Other, *specify*

TUMOUR THICKNESS (Note 11)

Specify ◯ mm
At least ◯

LYMPHOVASCULAR INVASION (Note 12)

- ◯ Not identified
- ◯ Indeterminate
- ◯ Present

Immunohistochemistry, *specify results if used*

TUMOUR-INFILTRATING LYMPHOCYTES (Note 13)

- ◯ Brisk
- ◯ Non-brisk

NON-NODAL LOCOREGIONAL CUTANEOUS METASTASES[c] (Note 14)

- ◯ Not identified
- ◯ Indeterminate
- ◯ Present

[c] *Satellite or in-transit cutaneous metastases.*

HISTOLOGICAL GROWTH PATTERN (Note 15)

- ◯ Circumscribed
- ◯ Infiltrative
- ◯ Other, *specify*

MARGIN/TISSUE EDGES STATUS (Note 16)

Peripheral margin

- ◯ Cannot be assessed
- ◯ Not involved by carcinoma

Distance from margin ◯ <1 mm

OR

mm to nearest 1 mm

Location, *specify if possible*

- ◯ Involved by carcinoma

Location, *specify if possible*

Deep margin

- ◯ Cannot be assessed
- ◯ Not involved by carcinoma

Distance from margin ◯ <1 mm

OR

mm to nearest 1 mm

Location, *specify if possible*

- ◯ Involved by carcinoma

Location, *specify if possible*

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LYMPH NODE STATUS (Note 17)

(Applicable only if lymph nodes submitted)

Sentinel lymph nodes

Number of sentinel lymph nodes examined

◯ Number cannot be determined

Number of involved sentinel lymph nodes

◯ Number cannot be determined

Extranodal extension

◯ Not identified
◯ Present

Maximum dimension of largest metastasis in sentinel node ___ mm

Location of largest sentinel node metastases (select all that apply)

☐ Subcapsular
☐ Intraparenchymal

Non-sentinel lymph nodes (clinically negative)

Number of non-sentinel lymph nodes examined

◯ Number cannot be determined

Number of involved non-sentinel lymph nodes

◯ Number cannot be determined

Extranodal extension

◯ Not identified
◯ Present

Maximum dimension of largest metastasis in regional node ___ mm

Clinically apparent lymph nodes

Number of lymph nodes examined

◯ Number cannot be determined

Number of involved lymph nodes

◯ Number cannot be determined

Extranodal extension

◯ Not identified
◯ Present

Maximum dimension of largest metastasis in regional node ___ mm

ANCILLARY STUDIES (Note 18)

◯ Not performed
◯ Performed, *record type of test(s) and result(s)*

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

PATHOLOGICAL STAGING (UICC TNM 9th edition)[d] (Note 19)

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

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

Primary tumour (pT)

◯ TX[e] Primary tumour cannot be assessed
◯ T0 No evidence of primary tumour
◯ Tis Carcinoma in situ
◯ T1 Tumour 2 cm or less in greatest dimension
◯ T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
◯ T3 Tumour more than 5 cm in greatest dimension
◯ T4 Tumour invades deep extradermal structures, i.e., cartilage, skeletal muscle, fascia or bone

Regional lymph nodes (pN)

◯ No nodes submitted or found
◯ NX[e] Regional lymph nodes cannot be assessed
◯ N0[f] No regional lymph node metastasis
◯ N1 Regional lymph node metastasis
  ◯ N1a (sn) Microscopic metastasis detected on sentinel node biopsy
  ◯ N1a Microscopic metastasis detected on node dissection
  ◯ N1b Macroscopic metastasis (clinically apparent)
◯ N2[g] In-transit metastasis *without* lymph node metastasis
◯ N3[g] In-transit metastasis *with* lymph node metastasis

[d] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 9th Edition, eds by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, Elizabeth Van Eycken. 2025, Publisher Wiley (incorporating errata published 12th October 2025).*

[e] *TX and NX should be used only if absolutely necessary.*

[f] *Histological examination of a regional lymphadenectomy specimen will ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.*

[g] *In-transit metastasis: a discontinuous tumour distinct from the primary lesion and located between the primary lesion and the draining regional lymph nodes or distal to the primary lesion.*

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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 P2 or above (based on the Hierarchy of Research Evidence for Tumour Pathology[1]). In rare circumstances, where level P2 evidence is not available an element may be made a CORE element where there is unanimous agreement in 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 P2 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 the DAC.

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Scope

This dataset has been developed for the reporting of the pathologic findings of primary cutaneous Merkel cell carcinoma (MCC) in excision (resection) specimens containing tumour. This dataset does not apply to partial superficial biopsies or re-excisions with no residual primary tumour. It is also not applicable for cytology specimens.

For small partial biopsies and cytology specimens, reporting the tumour diagnosis is usually sufficient. If there is no residual tumour seen in a re-excision, this should be reported. The features of the tumour seen in prior biopsies or excisions do not need to be repeated. In situations in which an initial partial (incisional or excisional) biopsy contains a substantial amount of tumour, completion of the dataset may require synthesising the findings of both the biopsy and subsequent excision with residual tumour.

A separate ICCR dataset is available for reporting invasive melanoma.[2]

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The second edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Skin Tumours, 5th edition, 2025.[3] In development of this dataset, the DAC considered evidence up until November 2025.

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)

For optimal tissue diagnosis and patient treatment, it is important that pathologists receive key clinical information with the specimen, especially information about the correct anatomic site.[4,5] Therefore, if relevant clinical information is received with the specimen it is a core element for reporting. However, in acknowledging that the pathologist is only capable of documenting the clinical information that they receive and that not all of it may be relevant, the clinical information sub-values (e.g., previous history of cancer) are non-core.

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Note 2 – Specimen(s) submitted (Core)

It is best practice to document the specimen(s) submitted as it provides critically important information for clinical review.

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Note 3 – Procedure (Core)

Reporting requirements vary depending on procedure type. Only a complete excision that includes the primary tumour can capture the full set of staging features. Therefore, reporting procedure type is considered core.

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Note 4 – Tumour site (Core)

Specification of the anatomic site of the tumour is crucial for ensuring clinical correlation, facilitating post-operative management decisions, and maintaining the accuracy of the patient's medical records.

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Note 5 – Macroscopic primary lesion description (Non-core)

The macroscopic description provides valuable information on the dimensions of the resected tissue and the size of the tumour. On occasion it may also help document the presence of a satellite. The macroscopic description is also helpful for assessing the margin status.

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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 should the need for internal or external review arise. If this information is not included in the final pathology report, it should be available on the laboratory computer system.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials. Indicate the most suitable block(s) for future ancillary studies.

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Note 7 – Tumour dimensions (Core)

Tumour diameter is a staging parameter.[6,7] Tumour diameter has historically been determined by clinical measurements. If that measurement is available, it should be reported as such. If clinical tumour diameter is unavailable, macroscopic and/or microscopic measurements should be used (largest diameter of tumour).

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Note 8 – Merkel cell polyomavirus (MCPyV) (Core)

The presence or absence of Merkel cell polyomavirus (MCPyV) segregates MCC into those of viral pathogenesis and those due to UV-mediated genetic damage.[8] These tumour subsets differ from one another genetically,[8,9] immunohistochemically,[10] and biologically.[11,12] MCPyV-negative tumours tend to be associated with worse outcome, hence this factor is of prognostic importance.[11,12] While sequence analysis may be used to test for the presence of the MCPyV, a more widely available method is immuno-histochemistry (IHC) using the antibodies CM2B4 or Ab3, both of which detect the MCPyV large T-antigen.[13] IHC for MCPvV, if available, is recommended for its prognostic value. It can also be helpful in diagnostically challenging cases.

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Note 9 – Histological tumour type (Core)

Merkel cell carcinomas (MCCs) should be classified according to the WHO Classification of Skin Tumours, 5th edition, 2025 (Table 1).[3]

Most MCCs exhibit a pure neuroendocrine phenotype. This histopathologic appearance is simply reported as MCC. Some tumours, however, display morphological diversity. They are commonly referred to as combined MCC. The most frequent combination is that of neuroendocrine and in situ and/or invasive squamous cell carcinoma,[14] identifiable on routine microscopy. However, the spectrum of morphologic diversity includes also adnexal differentiation, basal cell carcinoma, sarcomatoid and other lines of tumour cell differentiation.[14-16] Combined MCCs are mostly MCPyV-negative.[17.]

Table 1: 5th edition of the World Health Organization classification of tumours of the skin.[3]

Descriptor	ICD-O codes[a]
Keratinocytic/ependymal tumours	
Neuroendocrine carcinomas	
Merkel cell carcinoma	8247/3

[a] The morphology codes are from the International Classification of Diseases for Oncology (ICD-O).[18] 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.

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Note 10 – Extent of invasion (Core)

Documenting the extent of disease is relevant for staging (invasion of bone, muscle, fascia or cartilage constitutes pT4; except for superficial facial muscle involvement).[6,7] Indicating whether the tumour extends into superficial skeletal muscle or deep skeletal muscle can be of benefit.

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Note 11 – Tumour thickness (Non-core)

Tumour thickness is a reproducible/measurable parameter of potential prognostic significance.[19] When possible, if the specimen includes epidermis and dermis, tumour thickness is to be measured according to the method of Breslow and quantified in millimetres (mm) (rounded to the nearest 0.1 mm).

If a substantial portion of the tumour was removed by a prior procedure, the final report of residual tumour thickness should integrate information from the initial and subsequent specimens to provide the most accurate assessment of tumour thickness.

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Note 12 – Lymphovascular invasion (Core and Non-core)

Lymphovascular invasion (LVI) is prognostically relevant.[20] When lymphatic invasion is suspected, but not unequivocal on haematoxylin and eosin (H&E), the use of IHC (e.g., D2-40) should be considered to determine whether or not LVI is present or not. If IHC is used, this should be documented in the report.

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Note 13 – Tumour-infiltrating lymphocytes (Non-core)

Tumour-infiltrating lymphocytes (TILs) are potentially prognostically significant, especially if further stratified by immunophenotypic findings.[21-23,24] However, details of the tumour-associated lymphocytic infiltrate are currently not needed for routine clinical care and more work is needed for a standardised reporting scheme of proven prognostic significance, which is why for the time being TILs remain an optional data element for pathology reports.[21-24]

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Note 14 – Non-nodal locoregional cutaneous metastases (Core)

The presence of an in-transit metastasis indicates Stage N2.[6,7] Locoregional cutaneous metastases are metastatic tumour deposits affecting the anatomic region located between the primary tumour and regional lymph node basin. They may be detected clinically or only after microscopic examination. The metastatic deposits may involve the dermis, subcutis or skeletal muscle.

Metastases have historically also been designated *satellite* or *in-transit* lesions. Diagnostic and staging problems can sometimes occur.[25] A metastatic tumour to the dermis/subcutis may be confused with a second primary MCC or vice versa. A microscopic satellite lesion may be confused with part of the primary tumour that was artefactually separated from the mother lesion by surgery or regression. Therefore, for a suspected microscopic satellite to be accepted as bonafide metastasis it must be clearly separated from the main tumour by intervening normal tissue devoid of evidence of prior surgery or regression to avoid overdiagnosis.

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Note 15 – Histological growth pattern (Non-core)

An infiltrative growth pattern is found to be an adverse prognostic paramater.[26]

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Note 16 – Margin/Tissue edges status (Core)

It is core to record the presence or absence of tumour at the margins in the pathology report of a surgical excision with MCC. For reporting of the margin status, the DAC recommend a simple statement as to whether the margins are involved or not involved. While a pathologist may choose to measure the distance of the tumour to the nearest side or deep margin, providing such margin metrics is not needed for routine reporting, but the DAC encourage to report when tumour extends to within <1 mm of a tissue edge.

Recommendations for surgical margins for MCC are based on evidence that show clinical margins >10 mm are associated with improved overall survival and increase the odds for a histopathologically negative margin.[27]

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Note 17 – Lymph node status (Core and Non-core)

The number of involved lymph nodes has proven prognostic utility and should be recorded.[28] Lymph node involvement is the principal nodal staging determinant.[6,7] Metastatic MCC to lymph nodes is often readily identified on H&E-stained sections. However, it can be diagnostically challenging in the absence of a known primary tumour. Furthermore, the detection of rare tumour cells may be difficult and be facilitated by the use of IHC, such as for CK20.[29,30]

A positive node with microscopic disease is Stage pN1a and with macroscopic disease pN1b.[6,7] Only basic pN1 staging can be provided if this clinical and imaging information is not available to the pathologist at the time of reporting.

The DAC recommend reporting extranodal extension as non-core as it is an adverse prognostic feature.[6] While the recording of intranodal tumour size/burden is encouraged for investigational studies because of its potential prognostic significance, detailed metrics, such as the maximum diameter of metastatic deposit, are currently not staging criteria or needed for clinical care, which is why these data elements are not demanded.

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Note 18 – Ancillary studies (Non-core)

The use of IHC is recommended to confirm the diagnosis of MCC whenever the clinical and histopathologic findings are such that other tumours need to be considered in the differential diagnosis.

There is no one single immunohistochemical reagent that recognises all cases of MCC. Therefore, often a panel of antibodies is needed, the choice of which depends on the differential diagnosis of a specific case. Since CK20 expression is found in the majority of tumours, it is frequently employed in such panels, but various other antibodies may need to be used, especially for clinical presentations of metastatic MCC of unknown primary.[29-31]

Whichever immunostains are used for diagnosis, they and the respective results should be documented in the pathology report. IHC is also helpful for the detection of micrometastatic tumour deposits in sentinel lymph nodes.[29]

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Note 19 – Pathological staging (Core)

Staging data should be assessed according to the Union for International Cancer Control (UICC) 9th edition/American Joint Committee on Cancer (AJCC) 8th edition Cancer Staging Manuals.[6,7]

Primary tumour (pT)

Those patients with MCC in whom the primary tumour cannot be assessed (e.g., curetted) should be categorised as TX.[6,7] MCC in situ (i.e., completely limited to epidermis or adnexal epithelium) is categorised as Tis. The T category of MCC is classified primarily by measuring the maximum dimension of the tumour with a threshold of ≤20 mm (T1), >20 mm but ≤50 mm (T2), or >50 mm (T3). Extracutaneous invasion by the primary tumour into bone, muscle, fascia, or cartilage is classified as T4.

Regional lymph nodes (pN)

Regional metastases most commonly present in the regional lymph nodes. Nodal staging is primarily based on nodal tumour burden: microscopic versus macroscopic. Therefore, patients without clinical or radiologic evidence of lymph node metastases, but who have pathologically documented nodal metastases, are defined by convention as exhibiting 'microscopic' or 'clinically occult' nodal metastases. In contrast, MCC patients with both clinical evidence of nodal metastases *and* pathologic examination confirming nodal metastases are defined by convention as having 'macroscopic' or 'clinically apparent' nodal metastases.

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