The Royal College of Pathologists
Pathology: the science behind the cure

Standards and datasets for reporting cancers

Dataset for histopathological reporting of primary cutaneous malignant melanoma and regional lymph nodes

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Comments	This document will replace the 3rd edition first published in 2014. This is to incorporate the *TNM Classification of Malignant Tumours (8th edition)* from the Union for International Cancer Control (UICC) published in 2017. In accordance with the College's pre-publications policy, this document was on the College website for consultation from 6 September to 4 October 2018. Responses and authors' comments are available to view on request. **Dr Brian Rous** **Clinical Lead for Guidelines Review (Cellular Pathology)**

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NICE has accredited the process used by the Royal College of Pathologists to produce its cancer datasets. Accreditation is valid for five years from 25 July 2017. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

Foreword

The cancer datasets published by the Royal College of Pathologists (RCPath) are a combination of textual guidance, educational information and reporting proformas. The datasets enable pathologists to grade and stage cancers in an accurate, consistent manner in compliance with international standards and provide prognostic information, thereby allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. This guideline has been developed to cover most common circumstances. However, we recognise that guidelines cannot anticipate every pathological specimen type and clinical scenario. Occasional variation from the practice recommended in this guideline may therefore be required to report a specimen in a way that maximises benefit to the patient.

Each dataset contains core data items (see Appendix D1, D2, E1 and E2) that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Dataset) in England. Core data items are items that are supported by robust published evidence and are required for cancer staging, optimal patient management and prognosis. Core data items meet the requirements of professional standards (as defined by the Information Standards Board for Health and Social Care [ISB]) and it is recommended that at least 95% of reports on cancer resections should record a full set of core data items. Other non-core data items are described. These may be included to provide a comprehensive report or to meet local clinical or research requirements. All data items should be clearly defined to allow the unambiguous recording of data.

The following stakeholder organisations have been consulted during its preparation and have approved the dataset:

- British Association of Dermatologists (BAD; member of the RCPath Specialty Advisory Committee on Dermatopathology)
- British Society for Dermatopathology (BSD; member of RCPath Specialty Advisory Committee on Dermatopathology)
- National Specialist Dermatopathology External Quality Assessment (NSDEQA) scheme (member of the RCPath Specialty Advisory Committee on Dermatopathology).

This dataset has been constructed taking into account the strong evidence base that is contained in publications from the following national and international bodies/organisations. All publications have widespread national and/or international peer acceptance and reflect currently supported professional standards and practice in the diagnosis, management and treatment of cutaneous malignant melanoma:

- Union for International Cancer Control (UICC)[1]
- American Joint Committee on Cancer (AJCC)[2]
- World Health Organization (WHO) Classification of Skin Tumours[3]
- National Institute for Health and Clinical Excellence (NICE) Guidance and Quality Standards on skin cancer and melanoma[4–6]
- NHS Evidence[7]
- National clinical guidelines on melanoma published by the BAD with other professional bodies[8]
- International Collaboration on Cancer Reporting (ICCR)[9]
- European Organisation for the Research and Treatment in Cancer (EORTC)[10]
- Public Health England (PHE) Cancer Outcomes and Services Dataset (COSD)[11]
- NHS England Quality Surveillance Programme (QSP; formerly the National Cancer Peer Review Program)[12]

- Healthcare Improvement Scotland: Scottish Intercollegiate Guidelines Network (SIGN)[13]
- National Comprehensive Cancer Network (NCCN)[14]
- College of American Pathologists (CAP)[15]
- Armed Forces Institute of Pathology (AFIP) Atlas of Tumour Pathology (noting AFIP disestablished in 2011 and now under American Registry of Pathology [ARP] Press)[16]
- American Academy of Dermatology (AAD).[17]

Evidence for the revised dataset was obtained from updates to international tumour grading, staging and classification systems and by electronically searching medical literature databases for relevant research evidence, systematic reviews and national or international publications on uterine sarcomas. The level of evidence for the recommendations has been summarised (Appendix F). Unless otherwise stated, the level of evidence corresponds to 'Good practice point (GPP): Recommended best practice based on the clinical experience of the authors of the writing group'. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in Appendix G.

No major organisational changes have been identified that would hinder the implementation of the dataset, which will be fully integrated with future COSD versions, and there are no new major financial or work implications arising from the implementation, compared to the 2014 dataset.

A formal revision cycle for all cancer datasets takes place on a three-yearly basis. However, each year, the College will ask the author of the dataset, in conjunction with the relevant subspecialty adviser to the College, to consider whether or not the dataset needs to be updated or revised. A full consultation process will be undertaken if major revisions are required, i.e. revisions to core data items (the only exception being changes to international tumour grading and staging schemes that have been approved by the Special Advisory Committee on Cellular Pathology and affiliated professional bodies; these changes will be implemented without further consultation). If minor revisions or changes to non-core data items are required, an abridged consultation process will be undertaken whereby a short note of the proposed changes will be placed on the College website for two weeks for members' attention. If members do not object to the changes, the short notice of change will be incorporated into the dataset and the full revised version (incorporating the changes) will replace the existing version on the College website.

The dataset has been reviewed by the Clinical Effectiveness department, Lay Governance Group and Working Group on Cancer Services (WGCS) and was placed on the College website for consultation with the membership from 6 September to 4 October 2018. All comments received from the WGCS and membership were addressed by the authors, to the satisfaction of the Chair of the WGCS and the Clinical Lead for Guideline Review (Cellular Pathology).

This dataset was developed without external funding to the writing group. The College requires the authors of datasets to provide a list of potential conflicts of interest; these are monitored by the Clinical Effectiveness department and are available on request. The authors of this document have declared no conflicts of interest.

1 Introduction

1.1 Target users and health benefits of this guideline

The primary target users of this dataset are consultant and trainee cellular pathologists and biomedical scientists and, on their behalf, the suppliers of IT products to laboratories. Other target users are clinicians in secondary and primary care within the NHS and members of skin cancer multidisciplinary teams (MDT). Secondary users are NHS England and NHS Scotland, both involved in quality surveillance, cancer networks and those involved in skin

cancer data collection via the NHS, including PHE and in particular the National Cancer Registration and Analysis Service (NCRAS).

Standardised cancer reporting and MDT working reduce the risk of histological misdiagnosis and help to ensure that clinicians have all of the relevant pathological information required for tumour staging, management and prognosis. The collection of standardised cancer-specific data also provides information for epidemiologists and facilitates international benchmarking and research.

1.2 Purpose of the dataset

This document provides the dataset for the histological reporting of cutaneous malignant melanoma. It replaces the third edition of the previous dataset of 2014. Although the list of data items remains largely unchanged, in several instances their current usage has revised implications for staging and management of melanoma.

The meticulous diagnosis and reporting of cutaneous malignant melanoma is important because histological parameters play a major role in defining patient treatment. Similarly, recording of pathological parameters in the dataset has direct implications for the prognosis of individual patients. The use of datasets (and the background information that forms part of the datasets) in the context of the MDT meeting is advocated to optimise decisions related to patient treatment, to facilitate regular audit and review of all aspects of the service, to enable the collection of accurate data for NCRAS and to provide feedback for those caring for patients with cancer. It is important to have robust local mechanisms in place to ensure that the MDT clinical leads and NCRAS are apprised of supplementary or revised histology reports that may affect patient treatment and data collection.

1.3 Changes since the previous edition

The revised dataset is largely based on the format of the previous edition. The main alterations are as follows:

1.3.1 pTNM stage

UICC TNM 8, rather than AJCC TNM 8, has been selected by the RCPath because this provides staging of the entire skin surface for cutaneous squamous cell carcinoma, compared to just head and neck in AJCC TNM 8.[1,2] Although minor differences existed on publication between UICC TNM 8 and AJCC TNM 8, those for melanoma have now been corrected by UICC under website errata (www.wileyanduicc.com; www.cancerstaging.org).[18] UICC TNM 8 and AJCC TNM 8 now stage cutaneous melanoma identically. Caution has been applied in using the UICC prognostic grids as these remain based on UICC TNM 7 and have not yet been updated for TNM 8.

The main differences between TNM 7 and TNM 8 for cutaneous melanoma are summarised below.

pT category

Mitotic index no longer has a role in defining pT1a and pT1b subdivisions but remains a core prognostic indicator.

pT1a and pT1b division is now stratified at 0.8 mm, with or without ulceration. Thickness (Breslow thickness/depth) measurements are now measured to the nearest 0.1 mm (i.e. one and not two decimal points).

pN category

Lymph nodes are now defined as clinically occult (e.g. sentinel lymph node biopsy [SLNB]) or clinically apparent/detected. For N1a, N1b and N1c (SLNB), an indicator of tumour burden is

now recorded as a core but non-staging item (maximum dimension of the largest tumour deposit in millimetres).

A macroscopic entry relating to matted nodes is now required and when present is N3. New N1, N2 and N3 categories are introduced. N1c, N2c, N3c are introduced to accommodate satellite, microsatellite or in-transit metastases with either 0, 1 or ≥2 associated positive nodes, respectively.

M category
M1d representing central nervous system involvement is a new subdivision. When available, lactate dehydrogenase (LDH) receives a (0) or (1) suffix (non-elevated and elevated, respectively) for each M subdivision.

pTNM stage group
Pathological stage IA (with a pN0-negative lymph node biopsy) now includes pT1b and therefore carries a NICE recommended one year follow-up. If, however, there is no clinical nodal enlargement and SLNB has not been performed, it is recommended by the RCPath and BAD that this is regarded as clinical stage 1B and that the patient has a five and not one year follow-up.

Stage IIID is new to incorporate pT4b and N3.

1.3.2 Core and non-core data item

Data items are divided into core and non-core types.

As defined in the foreword, core items in RCPath cancer datasets are robust, evidence-based data items that are required for cancer staging, management and prognosis. These data items are expected to be available routinely for cancer MDT meetings, are recorded by MDT management systems and are used as part of the national QSP.

The foreword also sets out that non-core data items are not considered mandatory on a national basis, but some or all may be included to provide a more comprehensive report or to meet locally agreed clinical or research requirements.

The core pathological data items are summarised in structured proforma style, which may be used as the reporting format, or combined with free text as required. There is peer support for the idea that the use of structured proformas (or protocols/checklists) contributes substantially to improving the quality of histopathology reports.

Clark's level no longer has a role in melanoma TNM staging and is now recognised to have minimal additional prognostic value compared with the other core items available. On that basis, it has now become a non-core data item.

There is some debate as to whether tumour-infiltrating lymphocytes (TILs), regression and growth phase should also become non-core items. The entry, however, has kept its core designation in this edition, on the basis that TILs are still required when using the AFIP prognostic tables. Although the AFIP is now disestablished, the tables still enjoy reasonably widespread favour among clinicians.[19]

With informed patient choice based on verbal and written information given to all appropriate patients, NICE has recommended that SLNB is appropriate as a staging procedure for melanomas greater than 1 mm and stage IB–IIC. This advice is still consistent with the new staging in TNM 8.[5,6]

There is, however, considerable international debate regarding the most appropriate handling of SLNB and which data items should be recorded. To a degree, this is a circular argument, as the technical handling in clinical trials has been variable, thereby complicating

both prognostic and technical evaluation. Because of this, a pragmatic approach has been maintained for the dataset, recognising that the UK will probably continue to focus on clinical melanoma trials undertaken by the EORTC. For this reason, as in the previous edition, the RCPath continues to support the use of the EORTC protocol for SLNB handling.[10] If this protocol is not used, strategic clinical networks, clinical commissioning groups and NHS Trusts must be mindful that this could compromise trial entry for melanoma. The RCPath recommends that any alternative protocol has a detection rate of around 25%, although the evidence base for this remains limited in the absence of appropriate trials to address the question.

1.3.3 Changes in 2018

The authors are mindful that significant changes in the classification and management of skin cancer are likely to be published during 2018. These include a second edition of the WHO Classification of Skin Tumours and new national clinical guidelines on non-melanoma skin cancer from the BAD. Any such changes will be captured in the first revision of this dataset. After consideration, rather than await these changes, it was agreed that this new dataset would proceed to facilitate use of the new TNM classification from 1 January 2018.

2 Clinical information required on the specimen request form

Provision of clinical information is the responsibility of the clinician submitting a specimen for pathological examination. A range of clinical information, as indicated in the proposed UK National Histopathology Request Form (Appendix C), is required for both the COSD and MDT discussion relating to management, treatment and prognosis. The request form, although awaiting implementation, has been developed by PHE and endorsed by the BAD.

The minimum clinical items regarded as core for the pathology report are the site of origin of the specimen and the type of specimen. Other clinical items are considered important, but since their provenance is not the primary responsibility of the pathologist, they are listed as non-core items to encourage their collection and inclusion in the histology report.

3 Preparation of specimens before dissection

3.1 Skin specimens

The overall size of the specimen received must be measured. When appropriate, and in particular with excision specimens, this should incorporate three dimensions. Any unusual features that could be diagnostically important should also be recorded.

The presence, absence or any uncertainty about the existence of a lesion or abnormality to the naked eye must be recorded. When a lesion is apparent, measurements should include the maximum diameter and elevation.

Consideration should be given to inking the margins of all skin specimens with potential skin cancer. Standard techniques include the use of substances such as Indian ink, silver nitrate, crayon, alcian blue or commercial preparations. Excepting Mohs surgery, inking is the best way to obtain a reasonably accurate assessment of surgical margins and thereby lesional clearance. Discretion and flexibility should, however, be applied in this decision. The potential for dye to track and give rise to false margins should be taken into account in the final histopathological assessment. The routine inking of large specimens, especially with a clearly visible small central lesion, is debatable. Even in these circumstances, however, inking may be useful because of the possibility of unexpected microscopic extension of the lesion. It is not necessary to ink specimens that are submitted for diagnostic purposes, i.e. when there is no clinical intent to excise a lesion.

The examination of specimens submitted to the laboratory with prior designated orientation, by sutures or inking, for example, must be facilitated by the use of different coloured inks on different margins, notching the specimen or the insertion of coloured agar into the processing cassette. Alternatively, in a symmetrical specimen, only one margin needs be marked, as the inked and opposite margins can then be identified.

3.2 Lymph node specimens

3.2.1 Sentinel lymph nodes

SLNB is a very strong prognostic determinant and its use in staging is supported by both the UICC and AJCC. For England and Wales, in addition to its original recommendation for use in research and trial entry, NICE now recommends that SLNB should also be offered as a staging technique for melanomas greater than 1 mm in thickness[5] as part of informed patient choice. Currently, UK trials incorporating SLNB are likely to be EORTC based; thus, the RCPath continues to recommend use of the histological methodology that has been developed and used by the EORTC.[10] The evidence base for the EORTC protocol is one of the strongest currently available. In established units, alternative or EORTC-modified protocols are also acceptable outside EORTC clinical trials, provided that there is evidence of a positive detection rate approaching that of the EORTC protocol, i.e. an SLNB detection rate of around 25%. It should be noted that the positive detection rate of SLNB with the EORTC protocol can be up to 33%.[10,20] An overall detection rate of less than 20% is regarded as probably too low. It should be noted that the SLNB detection rate in the head and neck is often below 20% and multiple sentinel nodes may be identified. It is very clear, however, that more research is required to establish the most appropriate protocol, taking into consideration SLNB positivity, false-negative and false-positive rates, clinical outcome and the maximum size of metastasis, which has no significance in patient management. Studies are in progress that may reveal the minimum tumour burden below which a node can be regarded as effectively negative on a clinical basis.

3.2.2 Regional lymphadenectomy specimens

The generalities of macroscopic neck and axillary block dissection described for head and neck and breast apply equally to skin cancer.[21,22]

The overall dimensions of the fixed tissue must be measured, with particular note of any designated orientation and any apical node. Nodes should be identified by inspection and palpation. The use of clearing agents is time consuming and increases cost. Accordingly, although it assists in the identification of lymph nodes, it is not essential.

4 Specimen handling, dissection and block selection

4.1 Skin specimens

The method of handling excisional biopsies depends on the size of the specimen, whether the lesion can be seen, the position of the lesion on the specimen, the uniformity of the lesion and the type of processing technology. It is recommended that a separate judgement be made on each individual case, taking these variables into account, in the context of the following general comments.

Laboratories using rapid processing technology must ensure that trimmed tissue is no more than 2–3 mm in maximum thickness, whereas those using conventional processing technology can increase this to 4–5 mm.

For specimens that require trimming and in which the lesion can be seen, the specimen should be cut at regular intervals so that the nearest naked-eye margin to the lesion can be assessed histopathologically. For most skin ellipses, this will require transverse rather than

longitudinal sectioning. When multiple sections are required, this should be undertaken by the ‘sliced bread’ or ‘toast rack’ method.

The greater proportion of the specimen examined, the more accurate the assessment of the surgical margins will be. For macroscopically atypical melanocytic lesions or biopsy-proven melanoma, the whole lesion should be embedded and examined. When the lesion can be clearly identified, sampling the polar margins of skin ellipses can be discretionary and based predominantly on whether the lesion is close to the margin (under 1–2 mm) or less than that in the shorter transverse axis.

When the periphery of a pigmented lesion is indistinct, the whole of the specimen should be processed. In this situation, the polar ends from the long axis of a skin ellipse should be examined. These can be placed in one or two cassettes, depending on whether the specimen has been orientated clinically.

In some very large specimens, in addition to sampling the lesion, the peripheral margins at selected points (e.g. 3, 6, 9 and 12 o'clock) can be sampled, although the limitation in assessing margin clearance should be appreciated.

The dissection of a wedge excision (e.g. ear or lip) can be flexible depending on the nature of the specimen, whether there is a location marker and the position of the lesion. The same flexibility applies to whether the specimen needs to be inked. The selection of blocks taken, however, must be clearly documented and frequently a diagram can be useful. Additionally, if necessary, this should be accompanied by direct liaison between the person dissecting the specimen and the later reporting pathologist. This is the recommended approach to avoid potential problems in block interpretation during subsequent reporting. The blocks selected, however, must be able to measure the lesional margins to the same degree of accuracy stated in the dataset for the type of skin cancer present. Sometimes there is only one so-called wedge margin and no peripheral and deep margins. If applicable, the presence or absence of cartilage invasion should be stated in the report.

The requirement for step-levels/sections in any type of specimen is dependent on the margins. Requests for levels at cut-up can be used flexibly, but with the proviso that laboratory protocols and technical experience must ensure that sufficient material remains in the paraffin block for further investigation if subsequently proved necessary. The threshold for subsequently requesting step-levels in a difficult melanocytic lesion should be low.

Trimmed pieces of tissue of different thickness, or the processing of more than two pieces of tissue in one cassette, incurs an increased risk of incorrect orientation and sectioning with a potential loss of diagnostic and margin information.

Re-excision specimens are covered in section 11.5.

4.2 Lymph node specimens

4.2.1 Sentinel lymph nodes

The number of sentinel nodes for an individual nodal basin can be greater than one; for head and neck, not uncommonly, there may be several nodal basins. Each individual sentinel lymph node must be examined separately after fixation. Each lymph node should be partially freed from associated fat by careful dissection, leaving some fat so that the afferent lymphatics can be assessed for the presence of a tumour. Care must be taken not to damage the capsule or slice into the lymph node. The EORTC trial protocol (see section 3.2.1) requires the bivalve technique, in which a slice is made through the convex capsule and the hilum, along its longest meridian, to reveal two cut surfaces of the node. A bread-loaf technique using 2 mm sections is recognised to be equally sensitive in identifying nodal disease, but does not conform to the EORTC trial protocol. The whole of the two surfaces must be examined microscopically. Six pairs of sections are taken at 50 micron step intervals

for haematoxylin and eosin (H&E) and immunohistochemical (IHC) examination. In larger lymph nodes, the step sections should be increased to 100–400 micron intervals or greater to obtain deeper, more representative sampling. Spare sections from the second or third steps should be taken at the same time, numbered and stored so that if there is any problem with initial interpretation these can also be examined. The EORTC recommends the use of S100 as this is the most sensitive marker for melanoma, but the use of additional or alternative markers (such as SOX10, Melan A) is permitted if preferred. However, other markers are less sensitive and if used alone, the SLNB positivity rate should be audited and confirmed to be acceptable. Compared with other cancers, studies to date have shown that molecular methodology (PCR) is still insufficiently specific to be applied to melanoma. If a potential tumour deposit is seen macroscopically on either of the cut surfaces, this should be recorded and it may be sufficient to assess one H&E section and one adjacent section with immunohistochemistry.

4.2.2 Regional lymphadenectomy specimens

Each potential lymph node must be blocked, examined and recorded in a manner that permits an accurate count of node numbers and involvement at microscopy. Nodes can be bisected or sliced at 4–5 mm intervals. Representative sampling of a large (over 30 mm) mass of suspected lymph node(s)/tumour is acceptable, taking into account the necessity to identify the number of nodes, potential involvement and extracapsular invasion. The largest macroscopic lymph node and/or tumour mass should be described. The lymph node or tumour closest to the surgical margin, within a macroscopic distance of 5 mm, should be identified and sampled.

Matted nodes are two or more nodes that adhere to each other, identified at the time of specimen dissection in the laboratory, and their presence must be detailed in the pathology report. The presence of matted nodes signifies stage pN3 (see section 5.2.2)

Inking of the specimen surface is not essential.

If skin accompanies the specimen, any abnormal areas must be sampled. In the absence of a macroscopic abnormality, one random block of skin is adequate.

5 Core data items

5.1 Clinical

The site of origin and type of specimen are core clinical items for the pathology report.

In difficult cases, the provision of clinical photographs of the lesion or dermoscopy findings can be of diagnostic help by improving clinicopathological correlation.

The subdivisions of pN require knowledge of whether microscopically involved nodes are clinically occult or detectable and this information must be made available to the pathologist.

[Level of evidence B – The clinical status of lymph nodes – occult or detectable – is required for full pN staging.]

5.2 Pathological: macroscopic

5.2.1 Skin

The three-dimensional size of the specimen and the maximum diameter and elevation of all lesions must be recorded in millimetres. It must be recorded if the lesion is atypical to the naked eye. Atypical features include asymmetry, irregular border, variable colour/pigmentation and ulceration. Atypical features are also defined by the ABCDE criteria that are used commonly in public health education. These comprise Asymmetry, Border,

Colour, Diameter and Evolution. Consideration can be given to photography of atypical lesions, with a measurement scale.

5.2.2 Lymph nodes

The three-dimensional size of the overall surgical specimen must be recorded in millimetres and localising markers attached by the clinician should be noted. The presence or absence of dye in sentinel lymph nodes must be recorded to support its sentinel node status, and any macroscopic abnormality should be documented.

The identification of matted nodes during specimen dissection must be recorded and signifies nodal stage pN3.

[Levels of evidence – D and B.]

5.3 Pathological: microscopic

5.3.1 Histopathological subtype

The histopathological subtypes used in this dataset are as defined by the WHO[3] and are core dataset items in the National Clinical Guidelines (NCG) on cutaneous melanoma.[8]

The prognostic value of TNM 8 is based largely on nodular and superficial spreading subtypes of malignant melanoma.[1,2] It is acknowledged that apart from desmoplastic melanoma, the classic histogenetic subtypes of melanoma have debatable prognostic value, although lentigo maligna and acral lentiginous melanoma may have a different aetiology/pathogenesis and natural history. AJCC TNM 8 states that, at present, the same staging criteria should be used for melanomas with any growth pattern. However, the classic classification usefully highlights the myriad clinical and pathological guises of melanoma, which, if not recognised clinically and pathologically, can result in incorrect diagnoses. Desmoplastic invasive melanoma (± neurotropism) does appear, however, to have a different biological behaviour and outcome. Pure desmoplastic malignant melanoma (defined as having greater than a 90% desmoplastic component) has a better prognosis and reduced tendency for lymph node metastasis, but greater propensity for local recurrence. Mixed desmoplastic melanoma (with a desmoplastic component between 10 and 90%) has the same biological outcome as classic types of melanoma.

More recently, it has been recognised that different types of classic melanoma have different types and percentages of mutational abnormalities.[23] Although histological subtype does not replace mutational analysis, certain morphological subtypes can be useful predictors of potential mutational abnormalities. This is an important development in view of the introduction of specific targeted treatment for mutational abnormalities such as those involving the *BRAF* gene.

[Level of evidence C – Certain subtypes of melanoma have prognostic significance and some represent recognisable clinicopathological entities.]

5.3.2 Thickness (Breslow thickness/depth)

Melanoma thickness is a principal pT category parameter in TNM 8.[1] This is also a core data item in the NCG on melanoma, a site-specific item in the COSD and recommended by SIGN.[8,11,13]

As originally defined by Alexander Breslow, melanoma thickness constitutes an important prognostic factor for clinically localised primary cutaneous malignant melanoma. Increasing thickness signifies increasing metastatic risk and is correlated with decreased survival. It must be noted, however, that the correlation between thickness and prognosis is not absolute. A small number of patients with so-called ‘thin’ melanoma (usually defined as less than 1 mm) develop metastases and some with thick melanoma do not. Melanoma thickness

is a continuous variable and, accordingly, the even integers set in TNM 8 for staging are arbitrary and for practical convenience. Tumour thickness must be recorded in millimetres.

Thickness should be measured from the top of the granular layer or, when present and without any remaining epidermis, from the ulcer base to the deepest extent of invasion by a tumour cell or cells. Deep extension along periappendageal sheaths should be discounted. Microsatellites (defined in section 5.3.6) must not be included in the measurement of thickness. Regression, even if thicker than the viable melanoma, should not be included in the measurement but can be provided as a non-core item. Tumour thickness can be measured using a Vernier scale, eye-piece measuring graticule or measuring loupe. Where appropriate these must be calibrated to the microscope used for the measurement. In accordance with consensus recommendations, thickness measurements should be recorded (rounding up or down if necessary) to the nearest 0.1 mm, not the nearest 0.01 mm, because of the impracticality and imprecision of measurements, particularly for tumours over 1 mm^2. The convention for rounding decimal values is to round down those ending in 1 to 4 and to round up those ending in 5 to 9. If the base of melanoma in a section is transected by the surgical margin, the thickness should be qualified by the term ‘minimum’ or ‘at least'.

Tumour thickness can be evaluated accurately only in sections cut perpendicular to the epidermal surface. Nevertheless, in some tangentially cut specimens, it often is possible to report a tangentially measured thickness. The latter may be clinically useful because it may reasonably be inferred that the true tumour thickness would be no greater; this should be stated clearly in the pathology report. Sometimes, re-embedding the tissue may be successful in providing more perpendicular sections.

For primary melanomas lacking an epidermal component, the tumour thickness should be measured in the standard manner, from the top of the granular layer to the deepest invasive cell. For melanomas some distance away from the epidermal–dermal junction, including melanomas arising in congenital naevi or blue naevus-like melanomas, the tumour should be reported but with the qualification that it is not a conventional Breslow thickness.

The novel concept of Breslow density appears to have a useful prognostic value but it still requires additional independent study to confirm its validity. It can, however, be recorded as a non-core item.[24]

[Level of evidence B – Increasing tumour thickness correlates inversely with survival and is the principal pT stage parameter.]

5.3.3 Ulceration

Ulceration is a principal pT category parameter in TNM 8,[1,2] a core data item in the NCG on cutaneous melanoma, a site-specific data item in the COSD and recommended by SIGN.[8,11,13] Ulceration is now recognised to be a dominant independent prognostic factor for clinically localised primary cutaneous malignant melanoma. Survival rates for ulcerated invasive malignant melanoma are proportionally lower.[2] The extent of ulceration (defined either as diameter in millimetres or percentage of the whole lesion) adds more accurate prognostic information. There is early evidence to suggest that this is particularly so if the ulceration is greater than 5 mm in diameter or more than 70% of the lesion.

As in the previous melanoma dataset, ulceration is defined as the combination of the following features: full-thickness epidermal defect (including absence of stratum corneum and basement membrane at the epidermal–dermal junction), evidence of host reactive changes (i.e. fibrin deposition and neutrophils), and thinning, effacement or reactive hyperplasia of the surrounding epidermis in the absence of trauma or a recent surgical procedure.

[Level of evidence B – Ulceration is a major prognostic and pT stage parameter.]

5.3.4 Mitotic index

Mitotic index (rate) is no longer used as a T category criterion in TNM 8. The AJCC Melanoma Expert Panel, using the International Melanoma Database, have shown that ulceration and stratification at 0.8 mm were stronger predictors of melanoma-specific survival than mitotic rate.[25] It remains, however, a major determinant of prognosis across melanomas of all thickness. Accordingly, mitotic index must still be assessed and recorded in all primary malignant melanomas.[1,2] AJCC has indicated a highly significant correlation between an increasing mitotic index and declining survival rates; a mitotic index of 1 or more per mm^2 is a powerful adverse prognostic feature for melanoma.[2] Some still consider that mitotic index is the second most powerful prognostic indicator after thickness, and even greater than SLNB.

Mitotic index is a core dataset item in the NCG on melanoma, a site-specific item in the COSD and recommended by SIGN.[8,11,13] Despite use of the term mitotic rate by the UICC, AJCC and some other groups, the term mitotic index is used in this dataset. The terms mitotic index or mitotic count are preferred because they express more accurately what is meant by the pathologist (i.e. the proportion of cells that contain mitotic figures rather than the number of cells that enter mitosis per unit of time).

The AJCC provides specific guidance on measuring mitotic index.[2] The AJCC and the authors of this dataset acknowledge that there are areas of weakness in the methodology, but it is more important to adopt a clearly defined international approach for measuring mitotic index to facilitate research.

As the conversion between high power fields to mm^2 is variable, the number of high power fields that equate with 1 mm^2 must be calibrated for each individual microscope.

To enumerate mitoses, the TNM 8 guidance is that the area in the dermis containing the most mitotic figures should be identified first (the so-called 'hot spot').[2] After counting the mitoses in the 'hot spot', the count is extended to non-overlapping adjacent fields until an area corresponding to 1 mm^2 is assessed. If no 'hot spot' can be found and mitoses are sparse and randomly scattered throughout the lesion, then a representative mitosis is chosen and beginning with that field, the count is then extended to adjacent fields until an area corresponding to 1 mm^2 is assessed. The count, then, is expressed as the whole number of mitoses per mm^2. When the invasive component of a tumour is less than 1 mm^2 (in area), the number of mitoses present in 1 mm^2 of dermal tissue that includes the tumour should be enumerated and recorded as a whole number per mm^2, but not below 1/mm^2. If no mitoses are identified, the mitotic index should be recorded as none identified or 0/mm^2. In some institutions, when mitotic figures were not found after numerous fields were examined, the mitotic count was described as <1 mm.[2] This practice may be continued for research/trial data but is not regarded as the preferred way forward. It is recommended that no additional sections be cut and examined in excess of those that would normally be used to report and diagnose the melanoma to determine the mitotic index (i.e. no additional sections should be cut and examined for the sole purpose of determining the mitotic index, including in situations where no mitoses are identified on the initial routinely examined sections). IHC stains are not used for the purpose of identifying mitotic figures or index for reporting purposes.

[Level of evidence B – Increasing mitotic rate is a highly powerful indicator of reduced survival.]

5.3.5 Lymphovascular invasion and angiotropism

This is a primary tumour characteristic recommended for clinical care in AJCC TNM 8 and a core dataset item for the NCG on melanoma and the COSD.[2,8,11] The presence of lymphovascular invasion correlates with a worse survival in melanoma. The identification of an endothelial-lined space is an essential criterion for lymphovascular invasion, as it is essential to exclude retraction artefact. As indicated by the AJCC, it is not necessary to distinguish lymphatic and venous invasion. Lymphovascular invasion may correlate with SLNB positivity.

It appears that use of H&E sections often underestimates the degree of lymphovascular invasion, whereas this can be increased by using vascular markers such as D2-40. Such markers may be useful if there is uncertainty over whether a tumour is present in a vascular channel.

Angiotropism, defined as tumour cells surrounding a blood vessel, appears to have a bad prognosis but is rare.

[Level of evidence D – Presence of lymphovascular invasion correlates with a decreased survival.]

5.3.6 Satellite/microsatellite/in-transit metastases

Satellite/microsatellite/in-transit metastases are a principal pN category parameter in TNM 8.[1,2] N1c, N2c, N3c are defined by their presence plus the number of associated lymph nodes (0, 1 or 2 or more, respectively), irrespective of whether they are clinically occult or clinically detected. Satellite/microsatellite/in-transit metastases are a core data item in the NCG on melanoma, a site-specific item in the COSD and recommended by SIGN.[8,11,13] A satellite metastasis is defined by AJCC as being visible grossly in the skin or deeper tissue.[2] A microsatellite metastasis is defined as being visible only microscopically. Both satellites and microsatellites are defined as being present within 20 mm of the primary cutaneous melanoma. An in-transit metastasis is defined as being positioned more than 20 mm from the primary melanoma towards the regional nodes or acral proximity. The presence of satellites, microsatellites and in-transit metastases are associated with increased locoregional recurrence, a decreased disease-free survival rate and decreased overall survival.

TNM 8 provides only a limited histological definition for a microsatellite. Given their importance to staging, however, the RCPath regard it as unwise to leave open the minimum size of a microsatellite or the minimum distance from the main tumour. Accordingly, the RCPath support continuing use of the TNM 7 definition used in the previous edition of the melanoma dataset. Microsatellites were defined as any discontinuous nest of intralymphatic or possibly angiotropic metastatic cells greater than 0.05 mm in diameter and clearly separated by normal dermis (not fibrosis or inflammation) from the main invasive component of melanoma by a distance of at least 0.3 mm.

Although not yet formally published, there is widespread international peer agreement that microsatellites do not now have to be defined specifically as being contained within an identifiable endothelial-lined vessel. The RCPath supports this view.

It must be reported whether the margins for the satellite/microsatellite/in-transit metastasis are involved or not involved.[9]

[Level of evidence B – Satellite/microsatellite/in-transit metastasis is a principal pN category TNM stage parameter.]

5.3.7 Perineural invasion/neurotropism

Perineural invasion/neurotropism is a core data item for the NCG on melanoma and a primary tumour characteristic recommended for clinical care in AJCC TNM 8.[2,8] The definition of neurotropism includes the presence of melanoma abutting/around nerve fibres (perineural invasion) or within fibres (intraneural invasion). Occasionally, the tumour itself may form neuroid structures (termed neural transformation) and this is also regarded as neurotropism. Perineural invasion/neurotropism correlates with a higher recurrence rate. This is particularly common in desmoplastic malignant melanoma (so-called desmoplastic neurotropic melanoma) and may require wider excision margins.

There is little evidence to indicate whether the term perineural invasion/neurotropism in skin applies to intratumoral or extratumoral invasion, or invasion at the invading periphery/front of

the melanoma. Some restrict the term to the latter. The presence of tumour cells around nerves in the main mass of tumour caused by entrapment of nerves in the expanding tumour is not neural invasion. This information can be included as a non-core item.

In re-excision specimens it is important to ensure that apparent perineural invasion is not so-called 're-excision perineural invasion'. This reflects the presence of benign perineural epithelial cells in previously biopsied areas, most likely representing reactive/reparative proliferation of traumatised eccrine sweat gland ducts in a plane of lower resistance. Immunohistology can be used to make the distinction.

[Level of evidence C – Perineural invasion correlates with a higher local recurrence rate.]

5.3.8 Growth phase

Growth phase is an essential data item for the use of the AFIP eight-year survival prognostic tables[16] and is a core dataset item for the NCG on melanoma. It is supported as a data item by the AAD and recommended by SIGN.[8,13,17]

In basic terminology, malignant melanoma may be in situ (intra-epithelial or intra-epidermal) or invasive. There have been proposals to combine severe melanocytic atypia (dysplasia) with in situ malignant melanoma in a category designated melanocytic intra-epidermal neoplasia to minimise unnecessary categorisation of a spectrum of similar lesions.[26] To date, this has not received national or international endorsement but can be used as a non-core item. The growth phase model of tumour progression divides melanoma into those with radial or vertical growth phase. The model is of biological importance as those in the radial growth phase theoretically have no metastatic potential and a 100% survival rate. The model enjoys international usage and has been supported in many national and international working groups. Radial growth phase melanoma can have either an in situ or invasive component (so-called micro-invasive melanoma).

Growth phase is conceptually attractive but has problems in observer variation. Vertical growth phase melanoma is, by definition, always invasive. Vertical growth phase is defined by the presence of one or more suitably sized clusters or nests of melanoma cells within the dermis. Unfortunately, this has given rise to variable definitions in terms of the number of cells required in a nest to indicate that there is a vertical growth phase component. Although this point remains subjective, there is an increasing consensus in support of using a definition of more than ten cells across the diameter of a cluster. Similarly, a dermal nest that is larger than the largest intra-epidermal nest is considered evidence of vertical growth phase, but fails when the epidermal component is not nested. The presence of one mitotic figure within malignant dermal melanocytes indicates vertical growth phase but it must be emphasised that vertical growth phase can be present in the absence of identifiable mitotic activity. Tumour cells in the vertical growth phase divide and displace or compress the surrounding structures. In addition, the lymphocytic response is often less than that seen in the radial growth phase. Melanomas that invade into Clark level 3 and below are usually in the vertical growth phase and the tumours are often thicker than 1 mm. The term tumourigenic is synonymous with the term vertical growth phase. By comparison, the cells in an invasive radial growth phase are either solitary or in small clusters within the dermis. Increasingly, the latter is defined as below ten cells across the diameter of a cluster. Dermal mitotic figures are, by definition, absent in radial growth phase. The tumour cells often elicit a brisk lymphocytic response and the nests do not compress or distort the surrounding tissue. The lesions are usually thinner than 1 mm and are usually restricted to Clark level 2 in the invasive component. Non-invasive radial growth phase is the same as in situ malignant melanoma. Radial growth phase is synonymous with the term non-tumourigenic. These criteria have been found to be relatively reproducible when used by both experts and non-experts.

[Level of evidence D – Growth phase is used in one major survival model and is a core item in the NCG.]

5.3.9 Tumour-infiltrating lymphocytes

TILs are an essential parameter for use of the AFIP eight-year survival prognostic model.[16] They are an AJCC TNM 8 primary tumour characteristic recommended for clinical care,[2] a core dataset item for the NCG on melanoma, a site-specific data item in the COSD[8,11] and supported as a data item by the AAD.[17] TILs are a specific host immune response and could be regarded as the early sign of attempted regression. By definition, TILs must infiltrate the tumour and either disrupt or be apposed to the tumour cells.

The AFIP survival model defines three levels:

- absent – no lymphocytes within the tumour. This does not exclude peritumoral lymphocytes with no intratumoral extension and this is also called absent.
- non-brisk – focal/patchy/discontinuous lymphocytes among the tumour cells
- brisk – continuous infiltration among the entire peripheral element of the tumour or diffuse permeation within the tumour.

Although TILs are a diagnostic parameter in the AFIP eight-year survival model, there is continuing international debate with regard to their prognostic value. There is evidence that a paucity of TILs is an adverse survival factor and a brisk infiltrate a favourable prognostic factor. Some evidence has suggested that an absence of TILs maybe a predictor of a positive SLNB.

The assessment of TILs, however, remains subject to wide observer variation. A new method of assessing TILs, using a simplified numerical approach, has been suggested but this requires additional independent study to confirm its validity.[27]

[Level of evidence D – TILs are used in one major prognostic model, are a site-specific data item for COSD and in the national evidence-based guidelines.]

5.3.10 Regression

Regression is an essential diagnostic parameter in the AFIP eight-year survival model.[16] Regression is a core data item in the NCG on melanoma, a site-specific item in the COSD, supported as a data item by the AAD and recommended by SIGN.[8,11,13,17]

Despite its use in the AFIP survival model, debate continues as to its exact prognostic value. Some evidence correlates regression with a worse prognosis (especially in so-called thin melanomas), whereas other evidence has indicated a better prognosis. In particular, tumours with greater than 75% regression are said to have a much worse prognosis and may correlate with SLNB positivity. Some regard regression below 50% as focal and above 50% as extensive. Regression can be recognised by a combination of features:

- the variable destruction of melanoma cells with either a partial or nearly complete absence of tumour cells within the dermis
- a variable lymphohistiocytic infiltrate
- fibrosis
- increase in dermal blood vessels
- melanin-laden melanophages.

Sometimes the overlying epidermis is atrophic.

If regression is present to a greater depth than the Breslow thickness, regression depth is not added to the thickness measurement. A comment, however, can be added as a non-core item.

If dermal regression is present in a severely dysplastic naevus, in situ melanoma or invasive melanoma, there is some peer support, with appropriate skin cancer MDT discussion, for treating the lesion clinically as a potentially upstaged melanocytic lesion, taking the depth of dermal regression into account as potentially regressed invasive malignancy.

More research, however, is necessary to assess its exact significance.

[Level of evidence D – Regression is a site-specific data item in COSD and the NCG and is used in one major prognostic model.]

5.3.11 Margins

Local recurrence of primary cutaneous malignant melanoma and clinical morbidity is influenced by the completeness and adequacy of primary excision. In general, unless all of the margins have been examined, it is difficult to be certain about completeness of excision, so use of the words 'complete/incomplete' and 'adequate/inadequate' should be avoided in routine histopathological reports. The term 'complete' is more acceptable in the context of Mohs surgery, where the peripheral margin has been examined in its entirety. The term 'adequacy' implies a degree of clinicopathological judgement and is therefore applicable in the context of skin cancer MDT discussion. It is well recognised that in a significant number of cases where a tumour was reported to extend to an excision margin, there is no residual tumour on re-excision. This confirms that in such situations the term 'incomplete' can be inappropriate. Similarly, lesions not at the margin and seemingly 'complete' can occasionally recur clinically.

Although evidence is more robust for peripheral margins, there is broad peer consensus that comments about the histological clearance at both peripheral and deep excision margins are necessary. The word 'peripheral' rather than 'lateral' is preferred to avoid problems by an inferred medial element. The words 'lateral' and 'medial' may be appropriate in orientated specimens.

Measurements of the peripheral and deep margins of clearance at histological examination are required for clinical purposes and are core data items in the COSD. Tumour margins are recorded in COSD for skin cancer as follows:

- clearance by more than 5 mm
- clearance at or by more than 1 mm, but less than or equal to 5 mm
- clearance by less than 1 mm, but tumour does not reach the margin.[5]

The COSD, as a site-specific item, also requires a measurement of the final margin of excision of melanoma after a wide local excision procedure, and amalgamates clinical and histological data.[11] Guidelines on the surgical margins recommended for cutaneous melanoma are based on trials utilising clinical margins.[8] Histological margins are, however, widely used for melanoma as a surrogate marker for clinical margins in the context of skin cancer MDT. Knowledge of measured margins is also vital for undertaking skin cancer audits.

On this basis, this dataset recommends, as a core item, histologically measuring peripheral and deep margins for cutaneous invasive melanoma as involved (0 mm), less than 1 mm, or at and over 1 mm, to the nearest millimetre. This approach follows the recommendations in the first edition of this dataset. If present, the nearest peripheral margin for in-situ melanoma should also be recorded in cases of invasive melanoma. This is to cover the eventual adequate treatment of the invasive component, but potentially inadequate treatment of the in-situ component. This will highlight the issue clinically, which can then receive MDT management discussion.

Where necessary, the skin cancer MDT can use the measured histological margins as a surrogate for the clinical margins by taking into account tissue shrinkage. The amount of tissue shrinkage from the time of surgical excision to the time of examination of paraffin sections varies according to the type of tissue and cancer. Shrinkage of skin specimens is 10–20%. It is unclear whether this reflects the shrinkage of fresh tissue and/or the effect of formalin.[28,29]

There is increasing peer consensus that the accuracy of both margin status and invasion in lentigo maligna can be improved by the use of immunohistology (such as Melan A). The published evidence base, however, currently remains insufficiently strong to regard this as a routine requirement.

Deep margin assessment is required for pure in-situ melanoma because of the potential of adnexal extension (especially for lentigo maligna) to the deep margin.

[Level of evidence D – The extent of local margin clearance correlates with the risk of local tumour recurrence.]

5.3.12 Lymph nodes

Notes on the IHC diagnosis and diagnostic threshold of a nodal microscopic metastasis (micrometastasis) are provided in sections 11.2 and 11.3.

5.3.13 Number of regional nodes positive

The number of regional nodes positive for a metastasis is a primary determinant of pN stage. It is also a site-specific factor in the COSD.[2,11]

[Level of evidence B – The number of nodes involved is a principal pN staging determinant.]

5.3.14 Microanatomic location and tumour burden of micrometastases

A micrometastasis is a microscopic metastasis that is clinically occult and not clinically apparent/detectable. As discussed in section 11.3, there is currently no defined lower limit on size of a micrometastasis.

Studies have investigated micrometastatic parameters that predict nodal involvement in completion lymphadenectomy and/or improved patient survival. These have included microanatomic location, distance of micrometastasis from capsule, total percentage cross-sectional area of involvement and dimension of the largest micrometastasis. The parameter that may have the strongest correlation with nodal involvement on completion lymphadenectomy is the microanatomic location and pattern.[10,19] A positive SLNB with only subcapsular involvement is associated with a lower incidence of nodal involvement elsewhere. Parenchymal involvement is associated with a higher degree of nodal positivity and this increases with multifocal deposits (defined here as more than three). EORTC and AJCC both consider, however, that sentinel lymph node tumour burden is an important predictor of non-sentinel node positivity. Accordingly, both bodies have recommended that the maximum dimension of the largest discrete melanoma deposit in a sentinel node should be recorded in pathology reports, as best representing sentinel node tumour burden. This should be measured in millimetres and to the nearest 0.1 mm below 1 mm. AJCC states that to be considered a discrete deposit, the tumour cells must be in direct continuity with adjacent tumour cells.[2] CAP, in their melanoma protocol, similarly recommends the recording of tumour location and the maximum dimension of the largest deposit. In some instances, however, multiple small aggregates may be dispersed within a lymph node and separated by lymphoid cells. In these instances, the maximum dimension of the largest discrete deposit should still be recorded and not the area over which the multiple deposits are contained. It may be that multiple metastases with a slightly greater dimension are more significant than a single deposit of slightly greater dimension. However, the evidence for this remains unproven; accordingly, this aspect of assessment is listed as a non-core item. The

assessment of SLNB can be made on H&E sections and/or IHC sections stained with melanocytic markers.

Some modes of treatment for a positive sentinel lymph node status can be based on specified high-risk factors in sentinel node pathology. In addition to the number of positive nodes (three or more) or the presence of extranodal extension (see section 5.3.15), this also includes so-called extensive involvement of a sentinel node by metastatic melanoma. The term extensive is generally defined by modified Dewar criteria; namely, multifocal deposits (more than three microscopic metastases) or a single metstasis more than 5 mm in maximum diameter[10]

[Level of evidence C – Microanatomic location and pattern and tumour burden of a nodal micrometastasis on SLNB correlates with nodal involvement on completion lymphadenectomy.]

5.3.15 Extranodal/capsular extension

Extranodal/extracapsular extension (or spread/invasion) is widely regarded as a manifestation of potential biological aggression, is considered to be associated with a worse prognosis and prompts consideration of the use of adjuvant treatment. It must be distinguished histologically from metastases in afferent lymphatics. Its presence is defined by the extension of melanoma from the node through its fibrous capsule and into the surrounding fat.

[Level of evidence D – the presence of extranodal/capsular extension prompts consideration of adjuvant chemotherapy.]

5.3.16 Lymph nodes: highest/apical node

In lymphadenectomy specimens, clinicians frequently identify the highest/most apical lymph node. If identified, the report should state if this contains a metastatic deposit.

[Level of evidence D – This information is frequently requested by the clinician and considered to have some prognostic value.]

5.3.17 Molecular and/or cytogenetic investigations

These are usually requested after authorisation of the index melanoma report. The most frequent investigations are for BRAF mutations and fluorescence in situ hybridisation.

[Level of evidence A – Molecular and cytogenetic investigations have an established role in the diagnosis and management of melanoma.]

6 Non-core data items

Some or all of these data items may be included to provide a comprehensive report, and may be necessary for the local cancer alliance, clinical preferences or audit and research. These have originated as a result of their inclusion in national and international guidelines as non-core items or supported during informal consultation of the datasets.

6.1 Clinical

These are based on the NCG, core and site-specific items in COSD,[11] and the proposed UK National Histopathology Request Form (Appendix C). They also conform to NICE requirements[4–6] and can be captured if provided by the clinician. They include:

- grade of clinician undertaking procedure
- provision of clinical photograph or dermoscopy findings

- clinical diagnosis/description
- procedure intention of clinician (diagnostic or therapeutic biopsy)
- whether this is a tumour recurrence
- previous histology reference number(s)
- whether the patient is immunocompromised
- whether this is a tumour arising in an area of radiation or thermal injury, chronic draining sinus, chronic ulcer, chronic inflammation or Bowen's disease
- genetic predisposition.

6.2 Pathological: macroscopic

- Lesional photography.

6.3 Pathological: histological

6.3.1 Skin

- Clark level: the level of invasion, as defined by Wallace Clark, has been used for more than 40 years for various melanoma staging systems. Clark level no longer appears in TNM 8. AJCC state, however, that it is a primary tumour characteristic recommended for clinical care. Clark levels are defined as follows:
  - level 1: confined to the epidermis
  - level 2: tumour cells within the papillary dermis and/or periadnexal connective tissue sheath. The cells do not fill or expand the papillary dermis.
  - level 3: tumour cells fill and expand the papillary dermis. They form an almost curvilinear line at the interface between the papillary and reticular dermis. This is usually identified by the position of the superficial vascular plexus.
  - level 4: invasion of the reticular dermis
  - level 5: invasion of the subcutaneous fat.
- Other parameters:
  - diameter of ulceration or percentage surface ulceration of lesion
  - regression: if present, depth to nearest 0.1 mm and distance to nearest peripheral margin (involved, <1 mm, >1 mm, to nearest whole integer). A comment can be made if regression depth is greater than Breslow thickness.
  - subtypes: superficial spreading invasive melanoma can be divided into pagetoid or lentiginous subtypes, reflecting the nature of the epidermal component adjacent to the invasive nodule. Invasive lentiginous superficial spreading melanoma differs from lentigo maligna melanoma by the absence of significant actinic elastosis and little epidermal atrophy.
  - nuclear proliferation index as a percentage using an IHC marker such as Ki-67
  - lymphovascular/perineural invasion: if present, indicate whether this is intratumoral or extratumoral, and provide the distance to the resection margin (involved, or measure to the nearest mm as whole integer)
  - microsatellite/in-transit metastasis: if present, provide the distance to the nearest margin in millimetres (involved, or measure to the nearest mm as whole integer)
  - background naevus, whether present and if present whether dysplastic
  - actinic elastosis: if present, empirical grading of severity to correlate with sun exposure

- TNM stage group: minimum based on the information available
- Breslow density.[23]

6.3.2 Lymph nodes

- SLNB
  - distance from lymph node capsule to largest tumour deposit
  - number of subcapsular deposits (e.g. localised or multifocal).
- Completion/therapeutic lymphadenectomy
  - if margin clear: distance of tumour to nearest margin in millimetres
  - vascular invasion
  - mitotic index per mm^2 in the tumour deposit
  - nuclear proliferation index as a percentage in the tumour deposit
  - diameter of largest nodal metastatic deposit in millimetres, and specify whether more than 30 mm or 60 mm.

7 Diagnostic staging and coding

TNM and SNOMED are required for the COSD.[8]

7.1 pTNM stage and stage group

The pTNM stage categories are broadly condensed into four stage groups:

- stage 0: in situ
- stage I: localised disease
- stage II: more extensive localised disease
- stage III: regional nodal disease
- stage IV: metastasis.

Although pTNM classically refers to the anatomic extent of disease, more recently this has, at times, incorporated additional non-anatomic prognostic information giving rise to so-called prognostic groups (UICC) or prognostic stage groups (AJCC).

pTNM stage is based on three anatomical categories: pT (Tumour), pN (Node), M or pM (Metastasis).

- pT – Primary tumour
  - pTx: Primary tumour cannot be assessed
  - pTis: Carcinoma – in situ
  - pT has multiple subcategories, i.e. pT0, pT1, pT2, pT3, pT4, reflecting increasing pT stages
- pN – Regional lymph nodes
  - pN has multiple subcategories, i.e. pN0, pN1, pN2, pN3
  - for melanoma and Merkel cell carcinoma, isolated tumour cells are defined as N1
- M – Distant metastasis

- M/pM (if confirmed histopathologically) has two categories, i.e. M0, M1/pM1
- it should be noted that there is no MX nor pM0

- Additional descriptors can be used:
  - the suffix ‘m’ indicates the presence of multiple synchronous primary tumours in a single organ (i.e. skin) within four months of diagnosis and is recorded in parentheses, e.g. pT1 (m). The highest T category should be used. Beyond four months they are regarded as new metachronous tumours and staged separately.
  - the suffix 'sn' indicates SNLB and is shown in parentheses, e.g. pN1 (sn)
  - the prefix 'r' indicates a recurrent tumour with a disease-free interval or disease that has progressed with no interval. This can be designated ‘rp’ if based on pathological information.
  - the TNM R classification for residual tumour is not used as margin status; information is provided in more detail elsewhere in the dataset.

Full details are available in Appendix A.

7.2 SNOMED codes

SNOMED Topography (T) code should be recorded for the site.

SNOMED Morphology (M) code should be recorded for the diagnosis/tumour morphology.

SNOMED Procedure (P) codes should be recorded for the procedure. P codes vary according to the SNOMED system in use in different organisations; therefore, local P codes should be recorded and used for audit purposes.

However, it is noted that SNOMED is now in a practical transition phase as part of the intended full implementation by the NHS and PHE of SNOMED CT. SNOMED ceased to be licensed by the International Health Terminology Standards Development Organisation from 26 April 2017.

A list of applicable T and M SNOMED and SNOMED CT codes is provided in Appendix B. Mapping SNOMED CT terminology is provided.

8 Reporting of small biopsies

Small biopsies have only a very limited role in the diagnosis of cutaneous melanocytic lesions. They may sometimes have a diagnostic role in cosmetically sensitive or clinically difficult areas (e.g. on the face, digits) where a diagnosis could facilitate skin cancer MDT decision-making. This includes so-called mapping biopsies on the face for lentigo maligna, and conjunctival melanoma extending onto the cheek.

For suspicious nail lesions, it is essential that sufficient nail plate is removed to expose the lesion and the nail matrix should be included where appropriate, as melanoma arises from the matrix.[19]

For procedures with the clear intention of establishing only a diagnosis, data items for melanoma can be restricted to documenting whether there is in situ or invasive disease and for the latter, providing the minimum Breslow thickness. Any factors that are considered to increase the biological risk (e.g. perineural invasion) or affect treatment should also be included.

9 Frozen sections

Frozen sections have no role in the diagnosis of pigmented melanocytic lesions. The diagnosis should be based on paraffin-embedded tissue, permitting prospective skin cancer MDT discussion and patient involvement in any decision-making process.

Frozen sections have no role in lymph node assessment.

10 Cytological diagnosis

Cytology has no role in the index diagnosis of cutaneous melanoma.

Ultrasound and lymph node fine needle aspiration cytology, especially after sentinel node mapping, has a possible role in centres where full SLNB is not currently available.[8] The technique is less sensitive than SLNB.[8]

Fine needle aspiration and cytology is an appropriate modality to investigate clinically and/or radiologically abnormal regional lymph nodes for potential metastatic melanoma.

11 Specific aspects of individual tumours not covered elsewhere

11.1 Reporting pathologist

NICE and the NHS England QSP (previously the National Cancer Peer Review Programme) recommend that lymph node cytopathology and histopathology resulting from the investigation and treatment of primary cutaneous malignant melanoma should be undertaken by pathologists also involved in reporting cutaneous melanoma.[6,7,12] In particular, this is to improve the sensitivity and specificity of SLNB or equivalent (ultrasound and cytopathology) and to facilitate skin cancer MDT discussion and audit. For the same reason, it is not unreasonable for these aspects of cutaneous pathology to appear in postgraduate dermatopathology examinations and dermatopathology external quality assessment.

This NICE recommendation relates primarily to inguinal and axillary SLNB and lymph node dissections for skin cancer. Head and neck SLNB for skin cancer also lies within the competence of specialist dermatopathologists. These topics all lie within the area covered by the National Specialist Dermatopathology EQA. Lymph node dissection of the head and neck and associated reporting should, however, only be undertaken by those having appropriate skills and competence in the area. This is primarily demonstrated by regular practice in the field and participating in an appropriate EQA scheme. In general, this therefore limits head and neck lymph node dissection and reporting to individuals regularly involved in this area of head and neck pathology. Head and neck lymph node dissection should be undertaken and reported according to RCPath's neck dissection cancer datasets.[21]

NICE has recently recommended that selected patients with melanoma can now be offered SLNB for staging. This, however, has significant additional workload implications for histopathologists. Accordingly, it has been suggested that trained biomedical scientists (BMS) with proven skills, knowledge and competence may have a role in this area. In particular, it may be possible for BMS to screen the sentinel nodes and identify those that do and do not contain melanocytes. The latter group could then be reported as negative by the BMS and the former group passed to a histopathologist to report the nature of the melanocytes present. Exploratory studies in this area may be useful.

11.2 Immunohistochemical detection of micrometastases

Immunohistology should always be an adjunct to good quality H&E-stained sections. Although highly recommended, H&E staining alone is no longer mandatory for the purposes of identifying lymph node metastases and it is acceptable to classify node-positive metastases based solely on IHC staining for melanoma-associated markers. However, since some IHC markers are sensitive but not specific for staining melanoma cells (e.g. S100, tyrosinase), correlation and confirmation with H&E-stained morphology is essential. If doubt exists, confirmation with more specific melanoma markers (e.g. HMB-45, Melan A, SOX10) should be carried out. The latter melanoma markers are themselves of limited sensitivity and may not stain up to 30% of melanomas. S100 and SOX10 also have limited specificity and may stain other neural crest and myoepithelial cells. In several studies, however, the combination of permanent H&E sections with multiple levels and S100, Melan A and/or HMB-45 immunohistochemistry increases the overall diagnostic sensitivity of SLNB. The reverse transcriptase polymerase chain reaction (RT-PCR) technique is not regarded as sufficiently standardised or specific to warrant inclusion in the current diagnostic repertoire for nodal metastases.

11.3 Threshold for defining nodal micrometastases

There is no evidence to define a lower threshold of microscopically identifiable tumour burden that should be used to define node-positive disease for staging purposes. Evidence published in the melanoma literature demonstrates that even small volumes of metastatic tumour (e.g. deposits of 0.1 mm or less in diameter) are associated with a worse prognosis than pathologically negative nodes over time.[2] It is also stated that a lymph node in which any metastatic tumour cells are identified, irrespective of how few in number the cells are or whether they are identified on H&E or immunohistochemistry, should be designated as tumour positive.[2]

In essence, the TNM concept of isolated tumour cells, in common with Merkel cell carcinoma, does not apply to cutaneous melanoma in SLNB.

11.4 Skin cancer MDT referral

The following melanoma cases should be referred for local skin cancer MDT review:

- all patients with melanoma – primary, metastatic or recurrent
- patients with melanocytic lesions of uncertain but potential malignant nature
- cases to be considered for lymph node dissection or SLNB.[6]

The following melanoma/melanocytic cases should be referred for specialist skin cancer MDT review:

- patients with melanoma managed by other site-specific teams
- patients with melanoma stage group 2B or higher
- patients with melanoma stage group 1 or higher who are eligible for clinical trials
- patients with multiple melanomas
- patients younger than 19 years of age
- patients with metastatic melanoma
- atypical giant congenital naevi
- patients who need lymph node dissection or SLNB.[6]

11.5 Wider local excision specimens for melanoma

There has been considerable debate about the extent of histological examination required for wider local excision specimens for melanoma. The debate centres on the cost efficiency of examining macroscopically normal specimens when melanocytic abnormalities were absent from the margins of the index specimen(s). Some peers consider that this is the only way to ensure that residual disease or microsatellites/in-transit metastases are not overlooked. The identification of residual disease or microsatellites/in-transit metastases is particularly important, being integral to nodal staging.

Some pathologists also consider that the specimen should always be examined in its entirety with a BMS-led cut-up. Evidence suggests that in the absence of previous lesional tissue extending to the margins and no macroscopic abnormality, the likelihood of identifying residual melanocytic disease by processing the entire specimen is extremely low, but not zero.[30,31] An acceptable compromise would be to sample the specimen in its shortest transverse axis, incorporating the area where the scar appears closest to the margins. This can generally be achieved in one to four cassettes. There is considerable latitude for discretion in this area.

Clinicians need to know whether the specimen contains a scar and whether the scar is completely excised. Macroscopic examination is essential. This is the most reliable means of recording that the re-excision has been undertaken, while noting the dimensions of the wider excision specimen. The fixed specimen should be sliced every 2–4 mm to detect any macroscopic abnormalities such as potential satellites or in-transit metastases. If identified, these must be examined histologically and the margin status must be assessed.

There is increasing peer support for the use of IHC markers in the assessment of excision margins for both in situ and invasive melanoma of lentigo maligna type. In some departments, IHC is now used routinely in this situation. This is particularly so since the recognition of the new, so-called paucicellular variant of lentigo maligna melanoma. Although poorly described in the literature, this variant displays only low numbers of scattered, solitary atypical melanocytes or small clusters of slightly atypical melanocytes within the dermis. These can easily be misinterpreted as a non-specific inflammatory reaction; IHC is invariably required to establish the correct diagnosis.

If melanocytic abnormalities in the index specimen were reported to extend to the resection margins, the specimen should be examined more extensively. It is recommended that specimens up to 10 mm should be sampled in their entirety. Specimens over 10 mm can be sampled pragmatically according to the nature of the original margin involvement.

Involvement of the wider excision margin by melanoma similarly prompts consideration of the use of adjuvant treatment.

12 Criteria for audit

12.1 Audits recommended by NICE[6]

- Skin cancer excision margins between clinical specialties.
- Skin cancer specimens in primary care.
- Histopathology reporting times (see below).

12.2. Recommended by the RCPath as key performance indicators

See *Key Performance Indicators – Proposals for implementation* (July 2013) on http://www.rcpath.org/profession/quality-improvement/kpis-for-laboratory-services.html:

- cancer resections must be reported using a template or proforma, including items listed in the English COSD which are, by definition, core data items in RCPath cancer datasets. English Trusts were required to implement the structured recording of core pathology data in the COSD by January 2016 and to update their systems in line with subsequent COSD updates.
  - standard: 95% of reports must contain structured data
- histopathology cases must be reported, confirmed and authorised within seven to ten calendar days of the procedure
  - standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.

13 Acknowledgements

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The late A Bernard Ackerman MD is remembered for his infectious enthusiasm for dermatopathology and for facilitating intellectual thought in debating the necessity for, and content of, datasets/checklists/protocols.

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Appendix A UICC TNM 8 pathological staging of cutaneous malignant melanoma, regional lymph nodes and metastasis

Includes:

- eyelid
- penis and scrotum
- perianal skin (hair-bearing beyond 5 cm of anal margin)
- vulva
- external ear
- lip (hair-bearing skin).

Excludes:

- mucosal melanoma of head and neck
- mucosal melanoma of urethra, vagina, rectum and anus
- conjunctival and uveal melanoma.

The clinico-pathological implications of TNM 8 have been jointly reviewed by the BAD and RCPath.[32]

Definitions of TNM

Primary tumour (pT)

pTX	Primary tumour cannot be assessed (e.g. curettaged or severely regressed melanoma)
pT0	No evidence of primary tumour (e.g. unknown primary or completely regressed melanoma)
pTis	Melanoma in situ
pT1	Melanomas ≤1.0 mm in thickness
pT2	Melanomas >1.0–2.0 mm
pT3	Melanomas >2.0–4.0 mm
pT4	Melanomas >4.0 mm

Note: a and b subcategories/subdivisions of pT are assigned based on thickness (pT1) and ulceration as shown below:

pT classification	Thickness (mm)	Ulceration status
T1 – T1a – T1b – T1b	≤1.0 <0.8 mm 0.8–1.0 mm ≤1.0 mm	 a: without ulceration b: without ulceration b: with ulceration
T2	>1.0–2.0 mm	a: without ulceration b: with ulceration
T3	>2.0–4.0 mm	a: without ulceration b: with ulceration
T4	>4.0 mm	a: without ulceration b: with ulceration

Regional lymph nodes (pN)

pNX Patients in whom the regional nodes cannot be assessed (e.g. previously removed for another reason)

pN0 No regional metastases detected

pN1–3 Regional nodal metastasis based upon the number of metastatic nodes and presence or absence of regional intralymphatic metastases (in-transit or satellite and/or microsatellite metastases). The regional metastases can be clinically occult/microscopic (including SLNB) or clinically detected/macroscopic

N1–3 a–c subcategories are assigned as shown below:

pN classification	**Regional node**	**Intralymphatic metastasis**
pN1 One regional histologically involved node or regional intralymphatic metastasis with no regional involved node		
N1a	One node with microscopic metastasis(s) (clinically occult)	No
N1b	One node with macroscopic metastasis(s) (clinically apparent/detected)	No
N1c	No involved node	Yes
pN2 Two or three regional histologically involved nodes or regional intralymphatic metastasis with one regional involved node		
N2a	Two or three nodes with microscopic metastases (clinically occult)	No
N2b	Two or three nodes with at least one macroscopic metastasis (clinically apparent/detected)	No
N2c	One node with microscopic or macroscopic metastasis(s) (clinically occult or clinically apparent/detected)	Yes
pN3 Four or more regional histologically involved nodes or any number of matted nodes or regional intralymphatic metastasis with two		

or more involved nodes		
N3a	≥4 nodes with microscopic metastases (clinically occult)	No
N3b	≥4 nodes with at least one macroscopic metastasis (clinically apparent/detected) or any matted nodes	No
N3c	≥2 nodes with microscopic or macroscopic metastases (clinically occult or clinically apparent/detected)	Yes

Definition of regional node metastasis (cf distant metastasis): disease confined to one or more draining regional nodal basin(s). Those on the head and neck or trunk may have three or more regional basins.

The total number of involved nodes for pathological staging is the total of positive sentinel and non-sentinel nodes (identified after completion lymphadenectomy).

A microscopic metastasis (micrometastasis) is diagnosed after sentinel lymph node biopsy or completion lymphadenectomy (if performed). It occurs in the setting of no clinical abnormality, i.e. clinically occult.

A macroscopic metastasis is defined as a clinically apparent/detected nodal metastasis confirmed by therapeutic lymphadenectomy. It occurs in the setting of a clinical abnormality.

Matted nodes are identified during specimen dissection.

Intralymphatic metastasis: This may compromise a satellite or in-transit metastasis. A satellite is a macro- or micro-collection of cells within 2 cm of the primary tumour. An in-transit metastasis involves skin or subcutaneous tissue more than 2 cm from the primary tumour but not beyond the regional lymph nodes.

Isolated tumour cells are designated pN1.

Although not specifically stated in UICC8, there is broad agreement, which is supported by the RCPath, that pN2b and pN3b only require one positive clinically apparent/detected node among the overall total of positive nodes present.[2]

Distant metastasis (M)

M0 No distant metastasis

M1 Distant metastasis

M1a Metastasis to skin, soft tissue including muscle, or lymph nodes beyond the regional drainage

M1b Metastasis to lung

M1c Non-central nervous system (CNS) visceral sites

M1d CNS

Serum LDH is incorporated into the M category as a suffix:

(0) LDH – Not elevated

(1) LDH – Elevated

e.g. M1a (1) equals M1a with LDH elevated. No suffix is used if LDH is not recorded.

pTNM stage group

Stage	T	N	M
Stage 0	pTis	N0	M0
Stage I	pT1	N0	M0
Stage IA	pT1a	N0	M0
	pT1b	N0	M0
Stage IB	pT2a	N0	M0
Stage IIA	pT2b	N0	M0
	pT3a	N0	M0
Stage IIB	pT3b	N0	M0
	pT4a	N0	M0
Stage IIC	pT4b	N0	M0
Stage III	Any pT	N1, N2, N3	M0
Stage IIIA	pT1a, T1b, T2a	N1a, N2a	M0
Stage IIIB	pT0	N1b, N1c	M0
	pT1a, T1b, T2a	N1b, N1c, N2b	M0
	pT2b, T3a	N1, N2a, N2b	M0
Stage IIIC	pT0	N2b, N2c, N3b, N3c	M0
	pT1a, T1b, T2a, T2b, T3a	N2c, N3	M0
	pT3b, T4a	N1, N2, N3	M0
	pT4b	N1, N2	M0
Stage IIID	pT4b	N3	M0
Stage IV	Any pT	Any N	M1

Comment on stage and clinical follow-up of melanoma

For the clinical follow-up of melanoma, NICE recommended one year for stage IA and five years for IB and above.[5] This, however, was based on TNM 7 where pT1a and pT1b were in stage IA and stage IB, respectively. NICE guidance for TNM 8 is not currently available. In TNM 8, however, pathological stage IA, with a negative sentinel lymph node biopsy (pN0), now includes pT1b. This is clinically highly relevant in view of the NICE recommendation for a one-year and not five-year follow-up, as previously stated. The UICC TNM 8 stage for pT1b, with no clinical nodal

enlargement and when no sentinel lymph node biopsy has been undertaken, is not clearly stated in the UICC and AJCC TNM publications, although this is expected to be clarified in a new edition of the UICC TNM 8 Supplement (UICC Help Desk). In the interim, the BAD and RCPath consider it appropriate to interpret this situation as clinical stage IB and for the patient to have a five-year and not a one-year follow-up.[32]

Appendix B Cutaneous malignant melanoma SNOMED coding

Topographical codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Skin	T01000	Skin structure (body structure)	39937001
Lymph node	TC4000 (SNOMED 3) T08000 (SNOMED 2)	Structure of lymph node (body structure)	59441001

Morphological codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Primary cutaneous in situ malignant melanoma NOS	M87202	Melanoma in situ (morphologic abnormality)	77986002
Primary cutaneous invasive malignant melanoma NOS	M87203	Melanoma, no ICD-O subtype (morphologic abnormality)	2092003
Metastatic cutaneous malignant melanoma	M87206	Melanoma, metastatic (morphologic abnormality)	
Histological subtypes			
In situ			
Lentigo maligna	M87422	Hutchinson's melanotic freckle (morphologic abnormality)	61217001
Superficial spreading	M87432	No code	No code (use 77986002)
Invasive			
Nodular	M87213	Nodular melanoma (morphologic abnormality)	2142002
Lentigo maligna melanoma	M87423	Invasive melanoma in Hutchinson's melanotic freckle (morphologic abnormality)	44474009
Superficial spreading	M87433	Superficial spreading melanoma (morphologic abnormality)	55320002
Acral lentiginous	M87443	Acral lentiginous melanoma, malignant (morphologic abnormality)	16974005
Desmoplastic	M87453	Desmoplastic melanoma, malignant (morphologic abnormality)	51757004

Procedure

Local P codes should be recorded. At present, P codes vary according to the SNOMED system in use in different institutions.

Appendix C (Draft) UK National Histopathology Request Form for skin biopsies

Devised by the PHE Skin Site-Specific Reference Group and kindly provided for RCPath dataset information by PHE. Permission for use should be sought from the PHE. This histopathology request form has been approved by the BAD; the mode of national implementation is under consultation. This could be useful to ensure that the maximum clinical dimension of a lesion is always recorded.

The UK National Histopathology Request form for skin biopsies

Date of surgical procedure

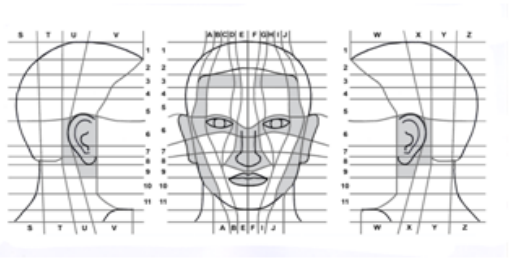
Please attach patient details

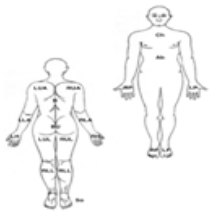
Name of surgeon

Grade of surgeon: Nurse, Specialist trainee, Consultant, Hospital Practitioner, Other

Clinical diagnosis: free text

Mandatory for Clinician to complete:	First biospy	Second	Third	Fourth
Site Code as per image (insert LUL etc)				
Clinical Diagnosis (select either BCC, SCC, Melanoma, Atypical Mole, other tumour or other). For inflammatory lesions add clinical details as free text.				
Clinical size of lesion sampled (max diameter) (mm)				
Intention of the surgeon (select *biopsy, excision or curative curettage*				
Procedure (select *curettage, shave biopsy, punch, incisional biopsy or excision)*				
For tumours give measured surgical clinical margin (mm)				
Is this a recurrent tumour?	Y/N	Y/N	Y/N	Y/N
Is the pateint immunocompromised?	Y/N			
Is this a tumour arising in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowen's Disease	Y/N	Y/N	Y/N	Y/N
Is this a tumour arising in a genetically predisposed individual?	Y/N			





Please mark site of samples taken on the above images For head and neck skin cancers the site code will be made up of the number in the horizontal grid and the letter from the vertical grid (e.g. for a tumour in the middle of the nose that might be code 8E). Where a lesion lies across grid lines then that grid reference in which the greater part of the tumour lies should be used OR if the lesion impacts on a grey shaded area or on the lips then that code should be used. Where the tumour is on the marked lips then the code LIP should be used. For tumours outside the head and neck the letters are indicated on the body map. e.g. a tumour on the left lower arm is LLA).

Free text

Appendix D1 Reporting proforma for cutaneous malignant melanoma

Surname…… Forenames……..… Date of birth…….. Sex…...
Hospital…….…….…… Hospital no…….…….. NHS/CHI no……..
Date of procedure…… Date of receipt……..…….. Date of reporting……...
Pathologist…….…… Surgeon…….…….. Report number ……..

Clinical data

Clinical site …….....

Specimen type*:

Not stated □

Incision Diagnostic □
Excision Diagnostic □ Therapeutic □ Uncertain □ Re-excision □ Wider local excision □
Punch Diagnostic □ Therapeutic □ Uncertain □
Curettings Diagnostic □ Therapeutic □ Uncertain □
Shave Diagnostic □ Therapeutic □ Uncertain □
Other □ Specify ….....

Macroscopic description

Dimensions of specimen: Length ……mm Breadth….mm Depth …….mm
Maximum diameter of lesion*: ..……..mm Uncertain □ No lesion seen □
Maximum elevation of lesion: ...……mm
Atypical features: No □ Yes □ Uncertain □ If yes: details.....

Histological data

NO INVASION i.e. IN SITU MELANOMA*

Histopathological subtype

Lentigo maligna □ Superficial spreading □ Acral lentiginous □

Not otherwise specified □ Other (specify) …….

Dermal regression: Not identified □ Present □ Uncertain □ Cannot be assessed □

Margins*

Peripheral: Involved □ Not involved but <1 mm □ Not involved ≥1 mm □ …..mm (to nearest 1 mm)
Uncertain □ Not applicable □

Deep: Involved □ Not involved but <1 mm □ Not involved ≥1 mm □ …..mm (to nearest 1 mm)
Uncertain □ Not applicable □

OR

INVASION PRESENT i.e. INVASIVE MELANOMA *

Histopathological subtype

Lentigo maligna melanoma □ Superficial spreading □ Nodular □

Acral lentiginous □ Desmoplastic □

Not otherwise classified □ Other (specify) ……

Breslow thickness (depth)* ..... mm

Ulceration*:
Not identified □ Present □ Uncertain □ Cannot be assessed □

Mitotic index*: …… mm^2

Lymphovascular invasion*:
Not identified □ Present □ Uncertain □ Cannot be assessed □

Microsatellite/in-transit metastasis*:
Not identified □ Present □ Uncertain □ Cannot be assessed □

Margin*:
Involved □ Not involved □ Uncertain □ Not applicable □

Neurotropic/perineural invasion:
Not identified □ Present □ Uncertain □ Cannot be assessed □

Growth phase: Radial (micro-invasive melanoma) □ Vertical □ Uncertain □

Tumour-infiltrating lymphocytes: Absent □ Non-brisk □ Brisk □

Regression:
Not identified □ Present □ Uncertain □ Cannot be assessed □

Margins*

In-situ component (if present);

Peripheral: Involved □ Not involved but <1 mm □ Not involved ≥1 mm □…..mm (to nearest 1 mm)
Uncertain □ Not applicable □

Invasive component:

Peripheral: Involved □ Not involved but <1 mm □ Not involved ≥1 mm □…..mm (to nearest 1 mm)
Uncertain □ Not applicable □

Deep: Involved □ Not involved but <1 mm □ Not involved ≥1 mm □…..mm (to nearest 1 mm)
Uncertain □ Not applicable □

---

pTNM* pT….. (UICC TNM 8)

SNOMED codes* .....

Comments

Pathologist…….. Date……..

*Data items that are part of the Cancer Outcomes and Services Dataset (COSD) version 8.

Appendix D2 Reporting proforma for regional lymph nodes associated with cutaneous melanoma

Surname…… Forenames……..… Date of birth…….. Sex…...

Hospital……..…….…… Hospital no…….. NHS/CHI no……..

Date of receipt…….…… Date of reporting……..…….. Report no……...

Pathologist……..…… Surgeon…….…… Date of surgical procedure ……..

Clinical data

Clinical site: Axillary □ Inguinal □ Other □

Laterality:* Right □ Left □

Clinical nodal status
- Clinically occult (SLNB/completion lymphadenectomy) □ or
- Clinically detected (therapeutic lymphadenectomy) □ or
- Clinical status unknown □

Macroscopic description

Sentinel lymph node biopsy

Dimensions of overall specimen …… mm x .....mm x .....mm

Macroscopic abnormality present: Not identified □ Yes □ If yes: maximum dimension*.....mm Uncertain □

Dye seen in tissue: Not identified □ Yes □

Localising marker: Not identified □ Yes □ If yes: details.....

Lymphadenectomy

Dimensions of specimen …….mm x .....mm x .....mm

Macroscopic abnormality present: Not identified □ Yes □ If yes: maximum dimension*.....mm Uncertain

Localising marker: Not identified □ Yes □ If yes: details.....

Matted nodes (stage pN3b) Not identified □ Yes □ Uncertain □

Histological data for nodes associated with cutaneous melanoma

Sentinel lymph node biopsy (clinically occult)

Number of sentinel nodes identified* ……..…

Number of nodes involved* ……

For each positive node:

Location and pattern of deposit(s)

Subcapsular only No □ Yes □

Parenchymal

Localised (≤3) No □ Yes □

Multifocal (>3) No □ Yes □

Tumour burden (maximum dimension of largest tumour deposit)

<0.1 mm Yes □ ..... or

0.1–1.0 mm (to nearest 0.1 mm) .....mm or

>1 mm (to nearest whole integer) .....mm

Extranodal/capsular extension No □ Yes □ Uncertain □

Completion lymphadenectomy (clinically occult)

Number of nodes identified* ……

Number of nodes involved* ……

Highest/most apical node involved: No □ Yes □ Not identified clinically □

Extranodal/capsular extension No □ Yes □ Uncertain □

Margin of specimen Involved □ Not involved □ Uncertain □ Not applicable □

Therapeutic lymphadenectomy (clinically detected)

Number of nodes identified* ……

Number of nodes involved* ……

Highest/most apical node involved: No □ Yes □ Not identified clinically □

Extranodal/capsular extension No □ Yes □ Uncertain □

Margin of specimen Involved □ Not involved □ Uncertain □ Not applicable □

---

pTNM pN*…. (UICC TNM 8) (NB: Need to summate SLNB and lymphadenectomy positive nodes)

SNOMED codes* ……..

Comments

Pathologist……... Date……..

Notes:

*Data items that are currently part of the Cancer Outcomes and Services Dataset (COSD) version 8.

Appendix E1 Reporting proforma for cutaneous malignant melanoma in list format

Element name	Values	Implementation comments
Clinical site	Free text	
Specimen type	Single selection value list: • Not stated • Incision, Diagnostic • Excision, Diagnostic • Excision, Therapeutic • Excision, Uncertain • Re-excision • Wider local excision • Punch, Diagnostic • Punch, Therapeutic • Punch, Uncertain • Curettings, Diagnostic • Curettings, Therapeutic • Curettings, Uncertain • Shave, Diagnostic • Shave, Therapeutic • Shave, Uncertain • Other	
Specimen type, Other, Specify	Free text	Only applicable if 'Specimen type, Other' is selected.
Dimension of specimen, Length	Size in mm	
Dimension of specimen, Breadth	Size in mm	
Dimension of specimen, Depth	Size in mm	
Maximum diameter of lesion	Size in mm	
Lesion dimension not given, reason	Single selection value list: • Uncertain • No lesion seen • Not applicable	Not applicable if value given for 'Dimensions of lesion'.
Maximum elevation of lesion	Size in mm	
Atypical features	Single selection value list: • No • Yes	

	• Uncertain	
Atypical features, details	Free text	Only applicable if 'Atypical features, Yes' is selected.
Histological subtype	Single selection value list: • IN SITU: Lentigo maligna • IN SITU: Superficial spreading melanoma in situ • IN SITU: Acral lentiginous melanoma in situ • IN SITU: Melanoma in situ, not otherwise specified • IN SITU: Melanoma, in situ, other • INVASIVE: Lentigo maligna melanoma • INVASIVE: Superficial spreading • INVASIVE: Nodular • INVASIVE: Acral lentiginous • INVASIVE: Desmoplastic • INVASIVE: Malignant melanoma, not otherwise classified • INVASIVE: Malignant melanoma, other	
Histological subtype, Other melanoma in situ, specify	Free text	Only applicable if 'Histological subtype, IN SITU: Melamona, Other' is selected.
Histological subtype, Other malignant melanoma, specify	Free text	Only applicable if 'Histological subtype, INVASIVE: Malignant melanoma, Other' is selected.
Breslow thickness (depth)	Size in mm	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Ulceration	Single value selection list: • Not identified • Present • Uncertain • Cannot be assessed	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Mitotic index	Number	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Lymphovascular invasion	Single value selection list:	Only applicable if an

	• Not identified • Present • Uncertain • Cannot be assessed	'INVASIVE' option is selected for 'Histological subtype'.
Microsatellite/in-transit metastasis	Single value selection list: • Not identified • Present • Uncertain • Not applicable	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Microsatellite/in-transit metastasis, Margin	Single value selection list: • Involved • Not involved • Uncertain • Cannot be assessed	Only applicable if 'Microsatellite/in-transit metastasis, Present' is selected.
Neurotropic/perineural invasion	Single value selection list: • Not identified • Present • Uncertain • Cannot be assessed	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Growth phase	Single value selection list: • Radial (micro-invasive melanoma) • Vertical • Uncertain	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Tumour-infiltrating lymphocytes	Single value selection list: • Absent • Non-brisk • Brisk	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Regression	Single selection value list: • Not identified • Present • Uncertain • Cannot be assessed	
Margins, Peripheral, In-situ component	Single selection value list: • Involved • Not involved but <1 mm • Not involved ≥1 mm	

	• Uncertain • Not applicable	
Margins, Peripheral, In-situ component, distance	Size in mm	Only applicable if 'Margins, Peripheral, In-situ component, Not involved ≥1 mm' is selected.
Margins, Peripheral, Invasive component, peripheral	Single selection value list: • Involved • Not involved but <1 mm • Not involved ≥1 mm • Uncertain • Not applicable	Only applicable if an 'INVASIVE' option is selected for 'Histological subtype'.
Margins, Peripheral, Invasive component, distance	Size in mm	Only applicable if 'Margins, Peripheral, Invasive component, Not involved ≥1 mm' is selected.
Margins, Deep	Single selection value list: • Involved • Not involved but <1 mm • Not involved ≥1 mm • Uncertain • Not applicable	.
Margins, Deep, distance	Size in mm	Only applicable if 'Margins, Deep, Not involved ≥1 mm' is selected.
pT category	Single selection value list: • X • 0 • 1a • 1b • 1c • 2 • 3 • 4	
TNM version	UICC8	UICC8 automatically selected.
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix E2 Reporting proforma for regional lymph nodes associated with cutaneous melanoma in list format

Element name	Values	Implementation comments
Clinical site	Single selection value list: • Axillary • Inguinal • Other	
Laterality	Single selection value list: • Right • Left	
Clinical nodal status	Single selection value list: • Clinically occult • Clinically apparent/detected • Clinical status unknown	
Specimen type	Single selection value list: • Sentinel lymph node biopsy • Completion lymphadenectomy • Therapeutic lymphadenectomy	
Dimension of specimen, dimension 1	Size in mm	
Dimension of specimen, dimension 2	Size in mm	
Dimension of specimen, dimension 3	Size in mm	
Macroscopic abnormality present	Single selection value list: • Not identified • Yes • Uncertain	
Maximum dimension of macroscopic abnormality	Size in mm	Only applicable if 'Macroscopic abnormality present, Yes' is selected.
Dye seen in tissue	Single selection value list: • Not identified • Yes	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected.
Localising marker	Single selection value list: • Not identified • Yes	

Localisation marker, details	Free text	Only applicable if 'Localising marker, Yes' is selected.
Matted nodes (stage pN3b)	Single selection value list: • Not identified • Yes • Uncertain	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic lymphadenectomy' is selected.
Number of sentinel nodes identified	Integer	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected.
Number of nodes involved	Integer	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected.
Positive SN[*n*], Subcapsular only	Single selection value list: • No • Yes	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected. Repeating data item – repeat *n* for each in 'Number of nodes involved'.
Positive SN[*n*], Parenchymal Localised	Single selection value list: • No • Yes	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected. Repeating data item – repeat *n* for each in 'Number of nodes involved'.
Positive SN[*n*], Parenchymal Multifocal	Single selection value list: • No • Yes	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected. Repeating data item – repeat *n* for each in 'Number of sentinel nodes involved'.
Positive SN[*n*], Tumour burden (maximum dimension of largest tumour deposit)	Single selection value list: • <0.1 mm • 0.1–1.0 mm • >1 mm	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected. Repeating data item – repeat *n* for each in 'Number of nodes involved'.
Positive SN[*n*], Tumour burden, size	Size in mm	Only applicable if 'Positive SN[*n*], tumour burden, 0.1–1.0 mm' or 'Positive SN[*n*], tumour burden, >1 mm' is selected. Repeating data item – repeat *n* for each in 'Number of nodes involved'.
Positive SN[*n*], Extranodal/capsular extension	Single value selection list: • No • Yes • Uncertain	Only applicable if 'Specimen type, Sentinel lymph node biopsy' is selected. Repeating data item – repeat *n* for each in 'Number of nodes involved'.
Number of nodes identified	Integer	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic

		lymphadenectomy' is selected.
Number of nodes involved	Integer	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic lymphadenectomy' is selected.
Highest/most apical node involved	Single value selection list: • No • Yes • Not identified clinically	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic lymphadenectomy' is selected.
Extranodal/capsular extension	Single value selection list: • No • Yes • Uncertain	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic lymphadenectomy' is selected.
Margin of specimen	Single selection value list: • Involved • Not involved • Uncertain • Not applicable	Only applicable if 'Specimen type, Completion lymphadenectomy' or 'Specimen type, Therapeutic lymphadenectomy' is selected.
pN category	Single selection value list: • X • 0 • 1a • 1b • 1c • 2a • 2b • 2c • 3a • 3b • 3c	
TNM version	UICC8	UICC8 automatically selected.
SNOMED codes	May have multiple codes. Look up from SNOMED tables.	

Appendix F Summary table – Explanation of levels of evidence

(modified from Palmer K *et al. BMJ* 2008;337:1832)

Level of evidence	Nature of evidence
Level A	At least one high-quality meta-analysis, systematic review of randomised controlled trials or a randomised controlled trial with a very low risk of bias and directly attributable to the target cancer type or A body of evidence demonstrating consistency of results and comprising mainly well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias, directly applicable to the target cancer type.
Level B	A body of evidence demonstrating consistency of results and comprising mainly high-quality systematic reviews of case-control or cohort studies and high-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in A.
Level C	A body of evidence demonstrating consistency of results and including well-conducted case-control or cohort studies and high-quality case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relation is causal and which are directly applicable to the target cancer type or Extrapolation evidence from studies described in B.
Level D	Non-analytic studies such as case reports, case series or expert opinion or Extrapolation evidence from studies described in C.
Good practice point (GPP)	Recommended best practice based on the clinical experience of the authors of the writing group.

Appendix G AGREE II compliance monitoring sheet

The cancer datasets of the Royal College of Pathologists comply with the AGREE II standards for good quality clinical guidelines. The sections of this dataset that indicate compliance with each of the AGREE II standards are indicated in the table.

AGREE standard	Section of guideline
Scope and purpose	
1 The overall objective(s) of the guideline is (are) specifically described.	1
2 The health question(s) covered by the guideline is (are) specifically described.	Foreword, 1
3 The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Foreword, 1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups.	Foreword
5 The views and preferences of the target population (patients, public, etc.) have been sought.	Foreword
6 The target users of the guideline are clearly defined.	1
Rigour of development	
7 Systematic methods were used to search for evidence.	Foreword
8 The criteria for selecting the evidence are clearly described.	Foreword
9 The strengths and limitations of the body of evidence are clearly described.	Foreword
10 The methods for formulating the recommendations are clearly described.	Foreword
11 The health benefits, side effects and risks have been considered in formulating the recommendations.	Foreword,1
12 There is an explicit link between the recommendations and the supporting evidence.	5,6
13 The guideline has been externally reviewed by experts prior to its publication.	Foreword
14 A procedure for updating the guideline is provided.	Foreword
Clarity of presentation	
15 The recommendations are specific and unambiguous.	2–11
16 The different options for management of the condition or health issue are clearly presented.	2–11
17 Key recommendations are easily identifiable.	2–11
Applicability	
18 The guideline describes facilitators and barriers to its application.	Foreword, 1
19 The guideline provides advice and/or tools on how the recommendations can be put into practice.	Appendices A–D
20 The potential resource implications of applying the recommendations have been considered.	Foreword
21 The guideline presents monitoring and/or auditing criteria.	12
Editorial independence	
22 The views of the funding body have not influenced the content of the guideline.	Foreword
23 Competing interests of guideline development group members have been recorded and addressed.	Foreword