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

Standards and datasets for reporting cancers

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

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Comments	This dataset has been revised to include updated references and changes to reporting proformas, including standardisation of terminology, SNOMED coding and clearer reporting division of *in-situ* and invasive melanoma (in particular to avoid confusion between the clinical terms 'lentigo maligna' and 'lentigo maligna melanoma'). In accordance with the College's pre-publications policy, this document was on the College website for an abridged consultation from 4–18 February 2014. Eighteen items of feedback were received. The authors considered them and amended the document as appropriate. Please email publications@rcpath.org if you wish to see the responses and comments. **Dr Suzy Lishman** **Vice-President for Advocacy and Communications**

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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 and allowing clinicians to provide a high standard of care for patients and appropriate management for specific clinical circumstances. It may rarely be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. The clinical risk of departing from the guidelines should be assessed by the relevant multidisciplinary team (MDT); just as adherence to the guidelines may not constitute defence against a claim of negligence, so a decision to deviate from them should not necessarily be deemed negligent.

Each dataset contains **core data items** that are mandated for inclusion in the Cancer Outcomes and Services Dataset (COSD – previously the National Cancer Data Set) 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 90% 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 organisations have been consulted during its preparation and have approved the dataset:

- British Association of Dermatologists (BAD) (as a co-institutional member of the RCPath Joint Specialty Advisory Committee on Dermatopathology)
- British Society for Dermatopathology (BSD) (as an institutional member of The Royal College of Pathologists' Joint Specialty Advisory Committee on Dermatopathology)
- National Specialist Dermatopathology External Quality Assessment Scheme (NSDEQA) (as a member of The Royal College of Pathologists' Joint Specialty Advisory Committee on Dermatopathology)
- National Cancer Intelligence Network (NCIN)
- Melanoma Study Group (MSG).

This dataset has been constructed taking into account the new strong evidence base that is contained in, and forms the basis of, the following new national and international publications. All publications have widespread national and/or international peer acceptance and reflect the current accepted professional standards and practice in skin cancer.

- COSD, previously the National Cancer Dataset, produced by NCIN[5]
- clinical guidelines published by the BAD and other professional bodies[6]
- World Health Organization (WHO) Classification of Skin Tumours[7]
- Armed Forces Institute of Pathology (AFIP) Atlas of Tumour Pathology[8]
- National Institute for Health and Clinical Excellence (NICE) Guidance on Cancer Series[9,10]
- National Cancer Peer Review (NCPR) Program by the Department of Health Cancer Action Team (CAT)[11]
- NHS Evidence[12]
- National Comprehensive Cancer Network (NCCN)[13]
- College of American Pathologists(CAP)[14]
- Royal College of Pathologists of Australasia (RCPA)[15]

- International Collaboration on Cancer Reporting (ICCR)[16]
- European Organisation for the Research and Treatment in Cancer (EORTC)[17]
- American Academy of Dermatology (AAD).[18]

As well as peer-reviewed scientific publications, consideration has also been given to published evidence and expert opinion on the internet, such as on Dermpedia (www.Dermpedia.com)

Evidence for the revised dataset was also obtained by electronically searching medical literature databases for relevant research evidence, systematic reviews and national or international publications on skin cancer up to November 2013. This identified no evidence to alter the views or conclusions of the publications listed above. The evidence has been evaluated according to the modified SIGN guidance and the level of evidence for the recommendations has been summarised according to College guidance (see Appendix E). Most of the supporting evidence is grade C or D or meets the GPP (Good Practice Point) criteria. No major conflicts in the evidence have been identified and any minor discrepancies between evidence have been resolved by expert consensus.

No major organisational changes have been identified that would hinder the implementation of the dataset, which is fully integrated with the COSD, and there are no new major financial or work implications arising from the implementation, compared to the 2002 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 sub-specialty 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 Specialty 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. All changes will be documented in the 'data control' section of the relevant dataset.

The dataset has been reviewed by the WGCS and was placed on the College website for an abridged consultation with the membership from 4–18 February 2014. All comments received from the WGCS and membership were addressed by the authors, to the satisfaction of the WGCS Chair and the Vice-President for Advocacy and Communications.

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.

1 Introduction

1.1 Purpose of the dataset

This document provides the dataset for the histological reporting of cutaneous malignant melanoma. It replaces the first edition of the previous dataset of 2002. Although the data items remain largely unchanged, in some instances their current usage has revised implications for treatment, management and prognosis of melanomas.

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 multidisciplinary team (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 Cancer Registries 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 Cancer Registries are apprised of supplementary or revised histology reports that may affect patient treatment and data collection.

1.2 Changes since the previous edition

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

a) Staging

It has been essential to accommodate the changes in the international staging of cutaneous malignant melanoma introduced in 2010. Ideally, staging of cutaneous malignant melanoma should be based on the latest published edition of the tumour, node and metastasis (TNM) categorisation of malignant tumours published by the International Union against Cancer (UICC).[1] Internationally it has been agreed that this should be identical to the same staging edition published by the American Joint Committee on Cancer (AJCC).[2] When published, however, it was clear that the UICC 7th edition contained significant errors in relation to skin cancer. Some of these remain unaddressed in the 4th edition of the *TNM Supplement.*[3] On that basis, after widespread consultation, the RCPath advised its members to use the AJCC 7th edition for Skin Cancer.[4] For the same reason, a similar decision was made by the NCIN.

An important change in the new AJCC 7th edition is the use of mitotic rate rather than Clark level for early melanoma staging. In this dataset, use of the term 'mitotic rate' is restricted to those instances where AJCC7 is cross-referenced or quoted directly. As explained in section 5.2.2 d, the term 'mitotic index' is considered to be more accurate and use of the latter term is therefore recommended in diagnostic practice. As indicated in section 5.2.2 d, the term 'mitotic count' is also acceptable, but not used in this dataset.

AJCC regards primary cutaneous staging as also applying to primary vulval, eyelid, penis and anal margin melanoma. ICD-O-3 topography codes listed by AJCC7 indicate that the dataset is similarly applicable to skin of lip, external ear and scrotum.

b) Core and non-core data items

In contrast to the first edition of this dataset, data items are now divided into core and non-core types as defined in the foreword. Core items in the 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 part of the Clinical Lines of Enquiry for the NCPR Program. Non-core data items are not considered mandatory but all or part may be included to provide a comprehensive report or to meet locally agreed clinical or research requirements. The core pathological data items are summarised in proforma style, which may be used as the main reporting format or may be combined with free text as required. The use of proformas and checklists significantly improves the quality of skin cancer histopathology reports.

c) Lymph nodes

In view of the greater use of sentinel lymph node biopsy and lymph node dissection, a new reporting proforma for nodal staging of melanoma has been included.

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 National Request Form, although awaiting implementation, has been developed by the NCIN and endorsed by the BAD.

The minimum clinical items regarded as core for the pathology report constitute the site of origin of the specimen and the type of specimen. Other clinical items are recognised to be 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 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, can 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.

3.2 Lymph node specimens

3.2.1 Sentinel lymph nodes

Sentinel lymph node biopsy (SLNB) is a very strong prognostic determinant and its use is supported both internationally and by the AJCC. For England and Wales, NICE recommends that SLNB should be undertaken in centres where there is experience of the procedure and preferably within the context of ethics committee-approved clinical trials.[9] Currently, UK trials incorporating SLNB are likely to be EORTC based and thus the RCPath recommends the histological methodology that has been developed and used by the EORTC.[17] 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 outwith EORTC clinical trials,

provided that there is evidence of a positive detection rate equivalent to that of the EORTC protocol, i.e. a SLNB detection rate of at least 25%, although up to 33% SLNB positivity can be detected with the EORTC protocol.[17] More research is required, however, to establish the most cost-effective protocol, taking into consideration SLNB positivity, false negative and false positive rates.

3.2.2 Regional lymphadenectomy specimens

The generalities of macroscopic neck and axillary block dissection described for head and neck and breast cancer (www.rcpath.org/publications-media/publications/datasets) apply equally to skin cancer.

The overall dimensions of the fixed tissue must be measured, with particular note of any designated orientation and, in particular, any apical node. Nodes should be identified by inspection and palpation. The use of clearing agents is time consuming and increases cost. Accordingly this is not regarded as 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 is made on each individual case, taking these variables into account, assisted by 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 many 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 more 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 (under 1–2 mm) to the margin or is 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, as well as sampling the lesion, the cruciate margins at 3, 6, 9 and 12 o’clock can be sampled, although the limitation in assessing margin clearance should be appreciated.

The requirement for step-levels/sections in any type of specimen is dependent on the requirement to identify a lesion, achieve full-face assessment, establish a diagnosis and assess 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 investigations if subsequently proved necessary. The threshold for subsequently requesting step-levels in a difficult melanocytic lesion should be very 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 resulting potential loss of diagnostic and margin information.

Re-excision specimens are dealt with 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 and occasionally there may be more than one nodal basin. 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 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 50µ step intervals for H&E and immunohistochemical examination. In larger lymph nodes the step sections should be increased to 100µ intervals or greater to obtain deeper, more representative sampling. Spare sections (usually eight) 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 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 to 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. Under these circumstances, it is acceptable in the first instance to examine the abnormality using routine H&Es and reassess the situation when the result is known.

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) matted 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.

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.

5.2 Pathological

5.2.1 Macroscopic

Specimen

a) Skin

The three-dimensional size of the specimen and the maximum diameter and height of all lesions must be recorded in millimetres. Record whether the lesion is atypical to the naked eye. Atypical features include asymmetry, surface irregularity or nodule development, irregularity of outline, variable pigmentation or apparent ulceration.

b) 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.

[Level of evidence D.]

5.2.2 Microscopy

a) Histopathological subtype

The histopathological subtypes used in this dataset are as defined by the WHO[7] and are core dataset items in the National Clinical Guidelines (NCG) on cutaneous melanoma.[6] The prognostic value of TNM7 is based largely on nodular and superficial spreading subtypes of malignant melanoma.[2] It is acknowledged that outwith desmoplastic melanoma, the classic histogenetic subtypes of melanoma have debatable prognostic value. The classic classification, however, highlights a myriad of clinical and pathological guises of malignant melanoma, which if not recognised clinically and pathologically can result in incorrect diagnoses. Desmoplastic, invasive malignant melanoma (+/- neurotropism) probably has a different biological behaviour and outcome. Pure desmoplastic malignant melanoma (defined as having greater than a 90% desmoplastic component) has a better prognosis, reduced tendency for lymph node metastasis but greater propensity for local recurrence. Mixed desmoplastic melanoma (with a desmoplastic component between 10–90%) has the same biological outcome as classic types of melanoma.

More recently, it has been recognised that different types of classic malignant melanoma have different types and percentages of mutational abnormalities.[19] 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.

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

b) Breslow thickness

Melanoma thickness is a principal T stage parameter.[2] This is also a core data item in the NCG on melanoma and a site-specific item in the COSD.[5,6] As originally defined by Alexander Breslow, melanoma thickness constitutes a vitally 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 survive. Melanoma thickness is a continuous variable and accordingly the even integers set in AJCC 6th and 7th editions for staging are arbitrary and for practical convenience. Tumour thickness must be recorded in millimetres, but AJCC7 does not state specifically whether this should be to one or two decimal places for all measurements. This is further complicated by AJCC7 using both possibilities in its pT staging definitions. The NCG and COSD recommend that thickness should be measured to the nearest one decimal place. This could, however, lead to incorrect staging at the pT1/2 (≤1.0/≥1.01 mm), pT2/3 (≤2.0/≥2.01 mm) and pT3/4 (≤4.0/>4.0 mm) boundaries. For example, a thickness of 1.01 mm is pT2 but if the measurement is taken to the nearest one decimal point and recorded only as 1.0 mm, this then reflects pT1. The authors therefore support the draft proposal of the ICCR,[16] which states that Breslow thickness should be measured to a minimum of one decimal place but at times to a greater degree of precision as to allow accurate AJCC staging. At the above staging boundaries, measurement to two decimal places will be required and must be recorded as such in the proforma to provide documented evidence for the allocated pT staging. Although not stated in the NCG and COSD, it is essential that the thickness in mm that is recorded in a database should accurately reflect the stated AJCC7 stage. A case could be made for recording the thickness only according to the four AJCC staging ranges, but there is strong national and international support for thickness to be recorded as individual measurements to support research. AJCC7 does not comment on the reliability of measurements in tissue susceptible to variable shrinkage during formalin fixation.

Thickness should be measured from the granular layer or, when present, the ulcer base, to the deepest extent of invasion by tumour cells. Deep extension along peri-appendigeal sheaths should be discounted. Microsatellites must not be included in the measurement of thickness. Regression, even if thicker than 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. If the base of melanoma in a section is transected by the surgical margin, the Breslow thickness should be qualified by the term 'minimum'.

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

c) Ulceration

Ulceration is a principal T stage parameter,[2] a core data item in the NCG on cutaneous melanoma and a site-specific data item in the COSD.[5,6] 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 diameter or more than 70% of the lesion.

AJCC7 notes on ulceration are summarised as follows.

Melanoma ulceration is defined as the combination of the following features: full-thickness epidermal defect (including absence of stratum corneum), evidence of 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.

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

d) Mitotic index

Mitotic rate is an important new primary determinant in AJCC7 for defining pT1b melanoma. Mitotic rate is a core dataset item in the National Clinical Guidelines on melanoma and is a site-specific item in the COSD.[5,6] AJCC7 indicates a highly significant correlation between an increasing mitotic rate and declining survival rates.[2] A mitotic rate of 1 or more per mm^2 is a powerful adverse prognostic feature for melanoma.[2]

Despite use of the term 'mitotic rate' by the AJCC and some other groups, the term 'mitotic index' is used in this dataset, as discussed in Section 1.2 a. The terms 'mitotic index' or '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).

AJCC7 provides specific guidance on measuring mitotic rate. The AJCC and the authors of the dataset acknowledge that there are areas of weakness in the methodology, but it is more important to adopt a clearly defined approach for measuring mitotic rate/index internationally in the interim to facilitate further research. The methodology will be 'fine tuned' in AJCC8.

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

The AJCC7 guidance is summarised below.

To enumerate mitoses, the area in the dermis containing the most mitotic figures should be identified first, the so-called 'hot spot'. After counting the mitoses in the 'hot spot', the count is extended to 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 number of mitoses per mm^2. For classifying thin ($\leq$1 mm) melanomas, the threshold for a non-ulcerated melanoma to be defined as T1b is $\geq$1 mitoses per mm.[2] When the invasive component of 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 number per mm^2. Alternatively, in tumours where the invasive component is <1 mm^2 in area, the simple presence or absence of a mitosis can be designated as at least $1/mm^2$ (i.e. mitogenic) or $0/mm^2$ (i.e. non-mitogenic). 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 historical data *but is not regarded as the preferred way forward.* AJCC states that it is common and appropriate practice with small, thin melanomas to have the technician place multiple sections cut from the block on a single slide. As a guide, it is suggested by AJCC that no more than two slides with such multiple sections be evaluated so that exhaustive evaluation of the lesion is not performed.

[Increasing mitotic rate correlates inversely with survival and is an important pT stage parameter – Level of evidence B.]

e) Lymphovascular invasion

This is a prognostic descriptor in AJCC7,[2] a core dataset item for the NCG on melanoma and the COSD.[5,6] 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. So-called angiotropism, with tumour cells surrounding blood vessels appears to have a particular bad prognosis.

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

f) Microsatellite/in-transit metastasis

Microsatellite/in-transit metastasis is a principal pN stage parameter in AJCC7.[2] Its presence signifies stage pN2c. Microsatellite/in-transit metastasis is a core data item in the NCG on melanoma and is a site-specific item in the COSD.[5'6] A satellite metastasis is defined by AJCC as being visible grossly;[2] a microsatellite metastasis is defined as being visible 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. The presence of satellites, microsatellites and in-transit metastasis are associated with increased locoregional recurrence, a decreased disease-free survival rate and decreased overall survival.

AJCC notes on microsatellites are summarised below.
These are defined as any discontinuous nest of intralymphatic metastatic cells greater than 0.05 mm in diameter that are 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 by AJCC, there is widespread international peer agreement that microsatellites do not now have to be defined specifically as being contained within an identifiable lymphatic vessel. The authors support this approach.

It must be reported whether the margins for the microsatellite/in-transit metastasis are involved or not involved.[16]

[Microsatellite/in-transit metastasis is a principal pN stage parameter – Level of evidence B.]

g) Perineural invasion/neurotropism

Perineural invasion/neurotropism is a core data item for the NCG on melanoma.[6] The definition of neurotropism includes the presence of melanoma around nerve fibres (perineural invasion) or within fibres (intraneural invasion). Perineural invasion/ neurotropism correlates with a higher recurrence rate. This is particularly common in desmoplastic malignant melanoma (so-called desmoplastic neurotropic melanoma).

There is no evidence to indicate whether the term ‘perineural invasion’ in skin applies to intratumoral or extratumoral invasion, or invasion at the invading front of the melanoma. Some, however, restrict the term to the latter. 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’ (RPI). 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.

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

h) Growth phase

Growth phase is a site-specific prognostic factor in AJCC,[2] a core dataset item for the NCG on melanoma, an essential data item for the use of the AFIP eight-year survival prognostic tables[6,8] and is supported as data item by the AAD.[18]

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 (MIN).[20] To date this has not received national or international endorsement. 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.[21] The model enjoys widespread 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).

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 to use a definition of more than 10 cells in a cluster. Similarly, a dermal nest which is larger than the largest intra-epidermal nest is considered evidence of vertical growth phase. 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 radial growth phase. Melanomas that invade into Clark level 3 and below are usually 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 10 cells in 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.

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

i) Tumour infiltrating lymphocytes

Tumour infiltrating lymphocytes (TILs) are an AJCC7 site-specific prognostic factor,[2] a core dataset item for the NCG on melanoma, a site-specific data item in the COSD[5,6] and supported as a data item by the AAD.[18] TIL status is an essential parameter for use of the AFIP eight-year survival prognostic model.[8] 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
- non-brisk – patchy/discontinuous lymphocytes in peripheral tumour cells or the middle of the tumour
- brisk – continuous infiltration around the periphery or 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 sentinel lymph node biopsy.

[Tumour infiltrating lymphocytes (TILs) are a site-specific data item for COSD and in the National Evidence Guidelines, and are used in one major prognostic model – Level of evidence D.]

j) Regression

Regression is stated to be a site-specific prognostic factor in AJCC 7,[2] a core data item in the NCG on melanoma, a site specific item in the COSD[5,6] and is supported as a data item by the AAD.[18] Regression is an essential diagnostic parameter in the AFIP eight-year survival model.[8]

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. 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
- melanin-laden melanophages.

If regression is present to a greater depth than Breslow thickness, regression is not included in the formal Breslow thickness measurement.

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

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

k) Clark level 4/5

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.

In AJCC7, 'mitotic rate' essentially replaces Clark level as the staging parameter defining pT1a versus pT1b, in the absence of ulceration. The only exception is when ulceration is absent and the mitotic rate cannot be measured. A Clark level of either 4 or 5 then categorises the melanoma as stage T1b.

[Clark level may be used as a p1b stage parameter – Level of evidence B.]

l) 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 and 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 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. In non-excision specimens (such as curettings), the term 'edge' may be a better term to use as 'edge' may not reflect the true surgical margin

Although evidence is more robust for peripheral margins, there is broad peer support 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 as follows:

- clearance by more than 5 mm
- clearance by more than 1 mm, but less than or equal to 5 mm
- clearance by less than or equal to 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.[5] Guidelines on the surgical margins recommended for cutaneous melanoma are based on trials utilising clinical margins.[6] Histological margins, however, are 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 melanoma as involved (0 mm), less than 1 mm, or at and over 1 mm, to the nearest mm. This approach follows the recommendations in the first edition of this dataset.

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.[22, 23]

There is increasing peer support 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 *in-situ* melanoma because of the potential of adnexal extension (especially for lentigo maligna) to the deep margin.

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

m) Lymph nodes

Notes on the immunohistochemical diagnosis and diagnostic threshold of nodal micro-metastases are provided in section 11.1.

Number of nodes positive

The number of nodes positive for micrometastasis or macrometastasis is a primary determinant of pN stage. It is also a site-specific factor in the COSD.[2,5]

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

Microanatomic location of micrometastases

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 and diameter of the largest micrometastasis. The parameter that has the strongest correlation with nodal involvement on completion lymphadenectomy is the microanatomic location.[17,24] A positive SLNB with only subcapsular involvement is associated with a lower incidence of nodal involvement elsewhere. Accordingly this is recommended as a core data item. Other parameters may be required in EORTC trials and these are listed in the non-core section.

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

Extracapsular invasion and specimen margin status

Extracapsular invasion (or spread/extension) 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 chemotherapy. It must be distinguished histologically from metastases in afferent lymphatics. Involvement of the specimen margin by melanoma similarly prompts consideration of the use of adjuvant radiotherapy.

[The presence of extracapsular invasion prompts consideration of adjuvant chemotherapy – Level of evidence D.]

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.

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

6 Non-core data items

All or some of these data items may be included to provide a comprehensive report, and may be necessary for local Cancer Network and clinical preferences, audit and research. These have originated as a result of their inclusion in national and international guidelines as non-core items or supported during earlier informal consultation.

6.1 Clinical

These are based on the National Clinical Guidelines[6], core and site-specific items in COSD[5] and the draft UK National Histopathology Request Form (Appendix C). They also conform to NICE requirements[9] and can be captured if provided by the clinician.

- Date of surgical procedure.
- Grade of clinician undertaking procedure.
- Clinical diagnosis/description.
- Procedure intention of clinician (diagnostic or therapeutic biopsy).
- Is this a tumour recurrence?
- Previous histology reference number(s).
- Is the patient immunocompromised?
- Is this 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

6.2.1 Macroscopic

Description:

- nodule: whether present or absent; if present: breadth and height
- border of lesion: regular or irregular
- pigmentation: uniform or variable
- symmetry.

6.2.2 Histological

Skin

- Diameter of ulceration and 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).
- Nuclear proliferation index as a % using an immunohistochemical marker such as Ki67.
- Lymphovascular/perineural invasion: if present, indicate whether this is intra-tumoural or extratumoural, 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.
- Cytogenetic results.
- Molecular results.
- TNM stage group: minimum based on the information available.

Lymph nodes

a) Sentinel lymph node biopsy

- Metastatic disease distribution:
  localised
  multifocal
  extensive.
- Size of largest metastatic deposit:
  < 0.1 mm
  0.1–1.0 mm (to nearest 0.1 mm)
  > 1 mm (to nearest whole integer).

b) 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 % in the tumour deposit
- Diameter of largest nodal metastatic deposit in mm, and specify whether more than 30 or 60 mm.

7 Diagnostic staging and coding

Staging and SNOMED coding are required for the COSD.[5]

7.1 pTNM status

pTNM status should be recorded according to the 7th edition AJCC.[2] TNM stage grouping should be deferred until all current staging information is available and if appropriate, until after skin cancer MDT discussion.

A stage group can be added to a histopathology report as a non-core item but the report should indicate that this is the minimum stage group based on the information in the report.

General principles

pT Primary tumour

pTx Primary tumour cannot be assessed

pTis Carcinoma *in situ*

pT1, pT2, pT3, pT4

Additional descriptors can be used:

The suffix ‘m’ indicates the presence of multiple primary tumours in a single site and is recorded in parentheses, e.g. pT(m) NM.

The ‘r’ prefix indicates a recurrent tumour when staging is carried out after a documented disease-free interval.

pN Regional lymph node status

pM Distant metastasis

Full details are provided in Appendix A.

7.2 SNOMED codes

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

SNOMED Morphology (M) code must 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.

A list of applicable T and M codes is provided in Appendix B.

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.[18]

For procedures with the clear intention of establishing only a diagnosis, data items for melanoma should be restricted to documenting whether there is *in situ* or invasive disease and for the latter, providing the minimum Breslow thickness. Any factors which are considered to increase the biological risk (e.g. perineural invasion) 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.[6] The technique is less sensitive than SLNB.[6]

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 NCPR 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. 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.[9,11] 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 sentinel lymph node biopsy and lymph node dissections for skin cancer. Head and neck sentinel lymph node biopsy 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, however, must 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 must be undertaken and reported according to The Royal College of Pathologists' neck dissection cancer dataset (www.rcpath.org/publications-media/publications/datasets/datasets-TP.htm).

11.2 Immunohistochemical detection of micrometastases

The AJCC7 notes in relation to this are summarised as follows.

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. The AJCC now considers it acceptable to classify node-positive metastases based solely on immunohistochemical (IHC) staining for melanoma-associated markers. Since some IHC markers are sensitive but not specific for staining melanoma cells (e.g. S100, tyrosinase), the definitive diagnosis must include detection with at least one melanoma-associated marker (e.g. HMB-45, Melan A/MART-1) if cellular morphology is not otherwise diagnostic. The specific melanoma markers are of limited sensitivity and may not stain up to 15% of melanomas. In several studies, however, the combination of permanent H&E sections with multiple levels and S100, Melan A and/or HMB-45, IHC increases the overall diagnostic sensitivity of sentinel lymph node biopsy. The reverse transcriptase polymerase chain reaction (RT-PCR) technique is not regarded as sufficiently standardised or specific to warrant inclusion in the diagnostic repertoire to currently diagnose nodal metastases.[2]

11.3 Threshold for defining nodal micrometastases

The AJCC7 notes in relation to this are summarised as follows:

There is no definitive evidence that defines a lower threshold of microscopically identifiable tumour burden that should not 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]

11.4 Skin cancer MDT referral

Melanoma cases to be referred for local skin cancer MDT review:[9]

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

Melanoma/melanocytic cases to be referred for specialist skin cancer MDT review:[9]

- 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
- patients with metastatic melanoma
- atypical giant congenital naevi
- patients who need lymph node dissection or SLNB.

11.5 Wider local excision specimens for melanoma

There has been considerable debate about the extent of histological examination that wider local excision specimens for melanoma require. 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 guaranteed way to ensure that residual disease or microsatellites are not overlooked. The identification of residual disease or microsatellites is particularly important as these would result in nodal upstaging.

Some pathologists also consider that the entire specimen should always be examined in its entirety with a biomedical scientist-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.[25,26] 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 to record that the re-excision has been undertaken and 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.

Although only a small published evidence base exists, 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 given 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 nonspecific inflammatory reaction and 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.

12 Criteria for audit of the dataset

Audits recommended by NICE:[9]

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

In keeping with the key performance indicators published by the Royal College of Pathologists (KPIs) (see *Key Performance Indicators – Proposals for implementation* (July 2013) on www.rcpath.org/clinical-effectiveness/kpi/KPI):

- 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 are required to implement the structured recording of core pathology data in the COSD by January 2014.

  Standard: 95% of reports must contain structured data

- Histopathology cases that are reported, confirmed and authorised within seven and ten calendar days of the procedure.

  Standard: 80% of cases must be reported within seven calendar days and 90% within ten calendar days.

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Appendix A AJCC7 pathological staging of cutaneous malignant melanoma, regional lymph nodes and metastasis

Includes: eyelid
penis and scrotum
anal margin and perianal skin
vulva
external ear
skin of lip.

Excludes: mucosal melanoma of head and neck
vaginal melanoma
conjunctival melanoma.

Definitions of TNM

Primary tumour (T)

TX Primary tumour cannot be assessed (e.g. curettaged or severely regressed melanoma

T0 No evidence of primary tumour

Tis Melanoma *in situ*

T1 Melanomas 1.0 mm or less in thickness

T2 Melanomas 1.01–2.0 mm

T3 Melanomas 2.01–4.0 mm

T4 Melanomas more than 4.0 mm

Note: a and b subcategories of T are assigned based on ulceration and number of mitoses per mm^2, as shown below:

T classification	Thickness (mm)	Ulceration status/mitoses
T1	≤1.0	a: without ulceration and mitosis <1/mm^2 b: with ulceration or mitoses ≥1/mm^2
T2	1.01–2.0	a: without ulceration b: with ulceration
T3	2.01–4.0	a: without ulceration b: with ulceration
T4	>4.0	a: without ulceration b: with ulceration

Regional lymph nodes (N)

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

N0 No regional metastases detected

N1–3 Regional metastases based upon the number of metastatic nodes and presence or absence of intralymphatic metastases (in transit or satellite metastases)

Note: N1–3 and a–c subcategories assigned as shown below:

N classification	Number of metastatic nodes	Nodal metastatic mass
N1	1	a: micrometastasis* b: macrometastasis*
N2	2–3	a: micrometastasis* b: macrometastasis** c: in transit met(s)/satellite(s) *without* metastatic nodes
N3	4 or more	In transit met(s)/satellite(s) *with* metastatic node(s)

Definition of regional node metastasis (cf distant metastasis): disease confined to one draining nodal basin or two continuous draining nodal basins.

* Micrometastases are diagnosed after sentinel lymph node biopsy and completion lymphadenectomy (if performed). They occur in the setting of no clinical abnormality.

** Macrometastases are defined as clinically detectable nodal metastases confirmed by therapeutic lymphadenectomy or when nodal metastasis exhibits gross extracapsular extension. They occur in the setting of a clinical abnormality.

Distant metastasis (M)

M0 No detectable evidence of distant metastases

M1a Metastases to skin, subcutaneous, or distant lymph nodes

M1b Metastases to lung

M1c Metastases to all other visceral sites or distant metastases to any site combined with an elevated serum LDH.

Note: Serum LDH is incorporated into the M category as shown below.

M classification	Site	Serum LDH
M1a	Distant skin, subcutaneous, or nodal mets	Normal
M1b	Lung metastases	Normal
M1c	All other visceral metastases	Normal
–	Any distant metastasis	Elevated

Anatomic stage/prognostic groups

Clinical staging*				**Pathological staging****			
Stage 0	Tis	N0	M0	0	Tis	N0	M0
Stage IA	T1a	N0	M0	IA	T1a	N0	M0
Stage IB	T1b	N0	M0	IB	T1b	N0	M0
	T2a	N0	M0		T2a	N0	M0
Stage IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
Stage IIB	T3b	N0	M0	IIB	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
Stage IIC	T4b	N0	M0	IIC	T4b	N0	M0
Stage III	Any T	≥N1	M0	IIIA	T1–4a	N1a	M0
					T1–4a	N2a	M0
				IIIB	T1–4b	N1a	M0
					T1–4b	N2a	M0
					T1–4a	N1b	M0
					T1–4a	N2b	M0
					T1–4a	N2c	M0
				IIIC	T1–4b	N1b	M0
					T1–4b	N2b	M0
					T1–4b	N2c	M0
					Any T	N3	M0
Stage IV	Any T	Any N	M1	IV	Any T	Any N	M1

* Clinical staging includes microstaging of the primary melanoma and clinical/radiologic evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

** Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy. Pathologic Stage 0 or Stage 1A patients are exception; they do not require pathological evaluation of their lymph nodes.

AJCC note on defining T1 melanomas

T1a is restricted to melanomas with three criteria:

1 ≤1.0 mm thick

2 Absence of ulceration

3 Mitotic rate 0 or <1 mm^2.

T1b melanomas are now defined as those whose tumour thickness is ≤1 mm and have at least 1 mitosis per mm^2 or tumour ulceration.

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	Malignant melanoma, no ICD-O subtype (morphologic abnormality)	2092003
Metastatic cutaneous malignant melanoma	M87206	Malignant 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	Malignant 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 NCIN Skin Site Specific Clinical Reference Group and kindly provided for RCPath dataset information by the NCIN. Permission for use should be sought from the NCIN. This histopathology request form is approved by the BAD; the mode of national implementation is under consultation.

The UK National Histopathology Request form for skin biopsies

Date of surgical procedure

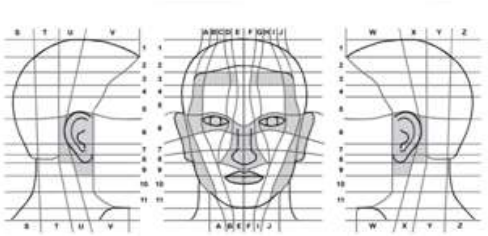
Please attach patient details

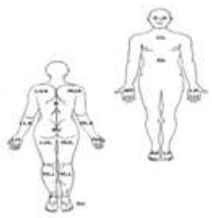
Name of surgeon

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

Clinical data

Clinical site …….....

Specimen type:

Excisional biopsy □ Incisional (diagnostic) biopsy □ Punch biopsy □ Shave □
Curettings (Diagnostic) □ Curettings (Excisional) □ Curettings (Not specified) □
Other (specify): ….…..……

Macroscopic description

Size of specimen: Length ……mm Breadth….mm Depth …….mm
Maximum diameter of lesion: ..……..mm Uncertain □ No lesion seen □
Maximum height of lesion: ...…….mm
Atypical features : No □ Yes □ Uncertain □

Histological data

NO INVASION i.e. IN-SITU MELANOMA

Histopathological sub-type

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 ..... 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 □ Vertical □ Uncertain □

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

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

Only if pT1a/b staging not possible from mitotic index and/or ulceration:

Clark level 4/5: No □ Yes □ Uncertain □ Cannot be assessed □

Margins

***In-situ* component:**

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

Invasive component:

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

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

TNM pathological (p) stage (AJCC 7) T…

SNOMED codes.....

Comments

Pathologist…….. Date……..

*** This can usually be recorded to the nearest one decimal place, but two places may be required at the pT1/2, pT2/3 and pT3/4 boundaries to achieve accurate pT staging.**

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……

Clinical data

Clinical site: Axillary □ Inguinal □ Other □

Localisation: Right □ Left □

Macroscopic description

Sentinel lymph node biopsy

Three-dimensional size: …… mm

Macroscopic abnormality present: No □ Yes □

Dye seen in tissue: No □ Yes □

Localising marker: No □ Yes □

Completion lymphadenectomy

Three-dimensional size: ……mm

Macroscopic abnormality: No □ Yes □

If yes, diameter of largest abnormality …….. mm

Localising marker: No □ Yes □

Histological data

Micrometastasis

Sentinel lymph node biopsy

Number of sentinel nodes identified ……

Number of nodes involved ……

For each positive node:

Location of deposit(s)

Subcapsular No □ Yes □

Parenchymal No □ Yes □

Extracapsular invasion No □ Yes □ Uncertain □

Completion lymphadenectomy

Number of nodes identified ……

Number of nodes involved ……

Highest/most apical node involved:	No □	Yes □	Not identified clinically □	
Extracapsular invasion	No □	Yes □	Uncertain □	
Margin of specimen	Involved □	Not involved □	Uncertain □	Not applicable □

Macrometastasis

Therapeutic lymphadenectomy

Number of nodes identified ……

Number of nodes involved ……

Highest/most apical node involved:	No □	Yes □	Not identified clinically □	
Extracapsular invasion	No □	Yes □	Uncertain □	
Margin of specimen	Involved □	Not involved □	Uncertain □	Not applicable □

TNM pathological (p) stage (AJCC 7) T…

SNOMED codes……...

Comments

Pathologist……... **Date……..**

Appendix E 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 F AGREE compliance monitoring sheet

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

AGREE Standard	Section of dataset
SCOPE AND PURPOSE	
1. The overall objective(s) of the guideline is (are) specifically described.	Foreword, 1
2. The clinical question(s) covered by the guidelines is (are) specifically described.	1
3. The patients to whom the guideline is meant to apply are specifically described.	1
STAKEHOLDER INVOLVEMENT	
4. The guideline development group includes individuals from all the relevant professional groups.	Foreword, 1
5. The patients' views and preferences have been sought.	Not applicable*
6. The target users of the guideline are clearly defined.	1
7. The guideline has been piloted among target users.	Previous editions and local use
RIGOUR OF DEVELOPMENT	
8. Systematic methods were used to search for evidence.	Foreword, 1
9. The criteria for selecting the evidence are clearly described.	Foreword, 1
10. The methods used for formulating the recommendations are clearly described.	Foreword, 1
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
13. The guideline has been externally reviewed by experts prior to its publication.	Foreword, 1
14. A procedure for updating the guideline is provided.	Foreword
CLARITY OF PRESENTATION	
15. The recommendations are specific and unambiguous.	3,4,5
16. The different options for management of the condition are clearly presented.	4,5
17. Key recommendations are easily identifiable.	3,4,5
18. The guideline is supported with tools for application.	Appendices A–D
APPLICABILITY	
19. The potential organisational barriers in applying the recommendations have been discussed.	Foreword, 1
20. The potential cost implications of applying the recommendations have been considered.	Foreword
21. The guideline presents key review criteria for monitoring and audit purposes.	12
EDITORIAL INDEPENDENCE	
22. The guideline is editorially independent from the funding body.	Foreword
23. Conflicts of interest of guideline development members have been recorded.	Foreword

* The Lay Advisory Committee (LAC) of The Royal College of Pathologists has advised that there is no reason to consult directly with patients or the public regarding this dataset because it is technical in nature and intended to guide pathologists in their practice. The authors will refer to the LAC for further advice if necessary.