

Standards and datasets for reporting cancers
Dataset for the histopathological reporting of uveal melanoma
(3rd edition)

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Authors: Dr Hardeep Singh Mudhar, Royal Hallamshire Hospital
Professor Sarah E Coupland, Royal Liverpool University Hospital

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Produced by	Dr Hardeep Singh Mudhar, Consultant Ophthalmic Histopathologist at Royal Hallamshire Hospital and member of the National Specialist Ophthalmic Pathology Service, and Professor Sarah E Coupland, Academic Head of Pathology/Honorary Consultant Lead of the Liverpool Ocular Oncology Research Group (LOORG) at the Royal Liverpool University Hospital, and member of the National Specialist Ophthalmic Pathology Service, on behalf of the College's Working Group on Cancer Services.
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The Royal College of Pathologists
2 Carlton House Terrace, London, SW1Y 5AF
Tel: 020 7451 6700
Fax: 020 7451 6701
Web: www.rcpath.org

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Contents

Foreword	3
1 Introduction	4
2 Clinical information required on the specimen request form	4
3 Preparation of specimens before dissection.....	5
4 Specimen handling and block selection	5
5 Core data items	7
6 Non-core data items.....	9
7 TNM pathological staging (7th edition UICC) ¹	10
8 SNOMED coding	10
9 Reporting of small biopsy specimens.....	10
10 Reporting of frozen sections	10
11 Specific aspects of individual tumours not covered elsewhere	10
12 Criteria for audit of the dataset.....	11
13 References	11
Appendix A TNM pathological staging of uveal melanoma (TNM 7th edition) ¹	14
Appendix B SNOMED codes.....	17
Appendix C Reporting proforma for uveal melanoma	19
Appendix D Proforma in list format	21
Appendix E Summary table – Explanation of levels of evidence	24
Appendix F AGREE compliance monitoring sheet	25



NICE has accredited the process used by The Royal College of Pathologists to produce its Cancer Datasets and Tissue Pathways guidance. Accreditation is valid for 5 years from July 2012. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

For full details on our accreditation visit: 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. 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 third version of this dataset has been produced after consultation and with approval from the following stakeholders: British Association for Ophthalmic Pathology (BAOP), the National Specialist Ophthalmic Pathology Service and UK ocular oncologists, working in the NHS Highly Specialised Services Commissioned Ocular Oncology Centres in Liverpool, London and Sheffield. In the previous round of consultation with members of the BAOP, whilst the separate recording of molecular prognostic data for uveal melanoma was agreed and highly recommended, the BAOP members felt that the dataset should just record histopathological prognostic data, in line with other RCPATH datasets.

Evidence for the data items in the dataset is derived from consensus of recognised experts together with review of current literature. Evidence has been graded using modified SIGN guidance – see Appendix E.

No major organisational changes or cost implications have been identified that would hinder the implementation of the 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 Fellows' attention. If Fellows 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.

This dataset has been reviewed by the Working Group on Cancer Services (WGCS) and was on the College website for consultation with the membership from 3 November to 1 December 2014. All comments received from the WGCS and membership were addressed by the author to the satisfaction of the WGCS Chair and the Vice-President for 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 Director of Clinical Effectiveness and are available on request. The authors of this document have declared that there are no conflicts of interest.

1 Introduction

This proposal for the reporting of uveal melanoma should be implemented for the following reasons:

- a) to ascertain staging of the disease
- b) to provide histological prognostic information
- c) to provide accurate data for cancer registration
- d) potentially to assist in selecting patients for future trials of adjuvant therapy
- e) to provide data for clinical audit and effectiveness
- f) to provide a database for research.

The synoptic proforma (Appendix C) is based on the *International Union Against Cancer/TNM Staging System (7th edition)*¹ and the *AJCC Cancer Staging Manual (7th edition)*.² Further guidelines on how to dissect ophthalmic specimens for the diagnosis of uveal melanoma can be found in the references at the end of this document.³

1.1 Target users and health benefits of this guideline

The target primary users of the dataset are trainee and consultant cellular pathologists and, on their behalf, the suppliers of IT products to laboratories. The secondary users are surgeons and oncologists, cancer registries and the National Cancer Intelligence Network. Standardised cancer reporting and multidisciplinary team (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. Collection of standardised cancer specific data also provides information for healthcare providers, epidemiologists, and facilitates international benchmarking and research.

2 Clinical information required on the specimen request form

- Age and sex of patient
- Laterality of eye operated on.
- Clinical findings.
- Previous therapy to enucleated/exenterated eye.
- Any history of systemic malignancy.
- Previous biopsies.

3 Preparation of specimens before dissection

Five types of specimens are likely to be received from patients with suspected uveal melanoma, usually in 10% buffered formalin. These are:

- iridectomies
- local resections of ciliary body/choroidal melanomas (with or without iris and trabecular meshwork)

- endo-resections
- enucleations
- exenterations.

Enucleations usually require 24 hours of fixation in 10% buffered formalin and exenterations usually 48 hours.

Sectoral iridectomy and localised resection specimens are often attached to a piece of sponge before receipt. The sponge keeps the specimen relatively flat and assists sectioning and preservation of planes for interpretation. If not, the specimen can be flattened between two cassette sponges overnight.

Endo-resections of intraocular tumours usually present as tiny fragments in a large volume of fluid in a vitrectomy discard container.

Occasionally, sutured Tantalum metal marker rings are seen over the scleral surface of enucleated eyes, indicating previous proton beam therapy. These are safe to handle and need to be removed prior to taking blocks. In some UK ocular oncology centres, the enucleation will have had a cap removed opposite the tumour or a sclerotomy flap immediately under the tumour; these indicate portals of entry to sample fresh tumour for molecular genetics analysis or research.

Orbital exenteration specimens are rarely done for uveal melanoma and may be complete or limited. Complete exenteration comprises removal of the eyelids, the globe, optic nerve, extraocular muscles, orbital fat and periosteum. For orientation purposes, the lashes of the upper lid are longer than those of the lower lid and the upper lid possesses a fold; the medial canthus possesses a caruncle and punctae.

4 Specimen handling and block selection

4.1 Macroscopic description

Iridectomy

The overall dimensions of the specimen and tumour are recorded. Painting the circumferential margins may facilitate orientation during microscopy.

Local resection

The specimen and tumour dimensions are recorded. The circumferential margins may be painted to facilitate measurement to the nearest margin at histology.

Endo-resections

The total volume of fluid is estimated, along with a description of the floating tissue fragments.

Enucleation

Enucleation specimens often have the following measurements made:

- antero-posterior globe diameter (normal 22–23 mm)
- horizontal globe diameter (normal 22–23 mm)
- vertical globe diameter (normal 22–23 mm).

The vortex veins are identified as they pass obliquely through the scleral canals.

If the globe does not have a sampling sclerotomy to disclose the location of the tumour, the globe should be transilluminated with a bright light source (fibre-optic). Any shadows are noted in terms of location and size, and may be outlined on the scleral surface by ink. The shadow usually corresponds to the location of the intraocular tumour. Any gross extraocular spread of tumour is noted and measured.

After sampling the vortex veins and optic nerve margin, the eyeball is usually sliced in the antero-posterior plane. The plane of section is dependent on the findings of external examination and transillumination. This will determine whether the initial slice will be horizontal, vertical or oblique. The idea is to usually end up with a central antero-posterior segment that includes the pupil, optic nerve and the main central bulk of the tumour (so-called 'PO' block).

The following observations are recorded after slicing the globe:

- the uveal compartments which are involved (iris/ciliary body/choroid)
- tumour height and base size (mm)
- evidence of extra-scleral invasion (mm)
- growth pattern: focal solid mass, diffuse, or 'ring' (i.e. extensive 360-degree anterior infiltration of the iridocorneal angle). with small tumours, it is sometimes better to determine the growth pattern histologically (see later)
- the intra-ocular structures that are involved by the tumour. with small tumours, it is often better to determine this histologically (see later)
- some authorities measure the location of the tumour from the ora serrata or optic disc edge.

Exenteration

Exenterations are usually performed in some cases of gross extra-ocular melanoma extension. The specimen usually has the following measurements made: maximum antero-posterior, horizontal and vertical measurements. Any relevant external features are described. The external soft tissue margins should be painted in suitable dye for margin assessment and orientation purposes. The specimen is usually 'bread-sliced' from side to side and the intraocular contents, along with any extraocular lesions, described as for an enucleation.

4.2 Block taking

Iridectomy specimens

- Main tumour with nearest margin.
- All circumferential margins sampled separately if possible.

Local resection of ciliary body and choroid

- Main tumour with nearest margin.
- All circumferential margins sampled separately if possible.

Endo-resections

- The fluid is spun down and the specimen handled as a paraffin cell block.

Enucleation specimens

- Optic nerve margin.
- Vortex veins.
- Main tumour block with pupil and optic nerve.
- Callotte/cap blocks if they contain tumour.

The optic nerve margin and vortex veins are sampled before slicing into the globe, to prevent contamination of these margins by tumour. A section of the optic nerve is taken, usually 3–4 mm behind its junction with the sclera; leaving a stump facilitates microtomy. The vortex veins are usually located 5–9 mm from the optic nerve, at 2, 5, 7 and 10 o'clock. However, there can be considerable variation in the number and locations of the veins. The vortex veins are cut transversely across, at the point where they exit the scleral canals. If a length of vortex vein is not demonstrable, some advocate making two parallel cuts into the scleral canal to, in effect, de-roof it and remove the vortex vein from the canal.

Vortex veins should be embedded longitudinally if possible, to maximise the chance of detecting intravascular invasion by uveal melanoma.

Exenteration specimens

For exenteration specimens, similar blocks to the above are taken, except that it will be difficult to obtain a vortex vein sample due to the presence of orbital soft tissue.

- Optic nerve resection margin.
- Tumour with the nearest orbital soft tissue and or cutaneous margins.

5 Core data items

5.1 Macroscopic data

Site of tumour

Iris melanoma is associated with a much lower mortality, compared to its ciliary and choroidal counterparts,^{5,6} and has a ten-times lower mortality compared to melanomas of other uveal sites.⁷ Ciliary body melanoma behaves comparatively worse than iris and choroid melanomas.^{1,8,9}

[Level of evidence B.]

Size of tumour

Tumour size (scleral basal diameter and maximum thickness [also termed 'height']) is an important prognostic factor for ciliary body and choroidal melanomas. The five-year mortality rates are 16%, 32% and 53% for small, medium and large tumours, respectively.^{10,11} The Collaborative Ocular Melanoma Study^{12,13} has defined the following size classification based on clinical measurements:

- small tumours: (tumour height 1–3 mm; scleral basal diameter more than 5 mm)
- medium tumours: (tumour height 2.5–10.0 mm and scleral basal diameter ≤16 mm)
- large tumours: tumour height ≥10 mm or scleral basal diameter diameter ≥16 mm; or >8 mm in maximum tumour height with optic nerve involvement.

In the 7th edition of TNM¹ and in the 7th edition of the *AJCC Cancer Staging Manual*,² a grid relating to TNM categories and how they relate to basal diameter and maximum tumour thickness for ciliary body and choroidal tumours only has been formulated (see reporting proforma and Appendix A). The AJCC classification of posterior uveal melanomas (tumour size category) is predictive of prognosis.¹⁴

The most accurate tumour measurements are usually made pre-operatively by ultrasound. If the melanoma has been sampled by the surgeon after the enucleation, one can only record the size of the residual mass.

[Level of evidence B.]

Extraocular extension

Transcleral extension carries a worse outcome compared to those melanomas confined to the eye.^{8,15-19} This can occur directly through the scleral collagen, perineurally, perivascularly or intravascularly into the emissary, vortex vein¹⁷ or aqueous blood vessels.

The 7th edition of TNM¹ and the 7th edition of *AJCC Cancer Staging Manual*² further subclassifies the size of the extraocular component as ≤5 mm or >5 mm.¹

[Level of evidence B.]

5.2 Microscopic data

Growth pattern of tumour

State whether the tumour is a focal solid mass, diffuse or of 'ring' type.

Diffuse uveal melanoma is defined as a tumour thickness of 20% or less than the greatest basal dimension.^{20,21} It grows along the choroidal plane with little focal elevation. Ring melanoma affects the anterior chamber angle and involves extensive circumferential growth along the trabecular meshwork and adjacent anterior chamber angle structures. Ring and diffuse patterns are associated with a worse prognosis and higher metastatic rate compared to a focal solid mass.²²⁻²⁵

[Level of evidence B.]

Cell types present

The modified Callender classification is used for determining cell type. This has prognostic significance for tumours of the choroid and ciliary body but not for iris.²⁶⁻²⁸ State whether the tumour is spindle, epithelioid or mixed.

Spindle A cells exhibit a slender oval nucleus, with a characteristic longitudinal nuclear groove, fine chromatin, an indistinct nucleolus and indistinct cytoplasmic borders. Spindle B cells shows a plumper open nucleus, coarse chromatin and a distinct eosinophilic nucleolus, with indistinct cytoplasmic borders. Epithelioid cells are polygonal, exhibit-marked nuclear pleomorphism, irregular nuclear contours, with coarse clumped chromatin, eosinophilic prominent nucleoli but with a distinct cytoplasmic border. There is no difference in prognosis between a spindle A or B cell²⁶⁻²⁸ and therefore calling a melanoma 'spindle' type (not otherwise specified) is acceptable. Spindle cell melanoma has a comparatively better outcome, compared with mixed and epithelioid melanomas.⁷ The prognosis worsens with an increase in epithelioid cell content.²⁶⁻²⁸

The American Joint Committee on Cancer (AJCC) has defined the histopathological tumour types with respect to cell types as follows:²

- spindle cell melanoma (> 90% spindle cells)
- mixed cell melanoma (>10% epithelioid cells and <90% spindle cells)
- epithelioid cell melanoma (>90% epithelioid).

[Level of evidence B.]

Extrascleral invasion

Quite often, microscopic extraocular invasion is detected that is not seen at gross examination.

Extraocular extension carries a worse outcome compared to those melanomas confined to the eye.^{8,15–19} This can occur directly through the scleral collagen, perineurally, perivascularly or intravascularly into the emissary, vortex vein¹⁹ or aqueous blood vessels.

The 7th edition TNM¹ and the 7th edition of *AJCC Cancer Staging Manual*² further subclassifies the size of the extraocular component as ≤5 mm or >5 mm.¹

Extraocular vortex vein invasion is associated with a choroidal location, large tumour size and adverse genetic tumour signatures.¹⁸

[Level of evidence B.]

Extracellular matrix patterns

On the largest tumour face, a Periodic Acid-Schiff stain (PAS) can be carried out, without counter stain, to assess the tumour extracellular matrix patterns.

Nine morphologic patterns of extracellular matrix deposition have been defined for ciliary body or choroidal melanomas.^{29–30} Most tumours have a heterogeneous PAS distribution. The presence of extracellular closed loops and networks (a network is defined as at least three back-to-back closed loops) is a feature strongly associated with death from metastatic disease.^{30–32}

[Level of evidence B.]

6 Non-core data items

Macroscopic

Size of specimen/tumour.

Microscopic

Mitotic rate.¹¹

Tumour necrosis.³³

Presence of melanin pigmentation.¹¹

Density of lymphocytic infiltration.^{34–35}

Breach of Bruch's membrane.³⁶

Optic nerve extension.^{11,16,37}

7 TNM pathological staging (7th edition UICC)¹

The recommendation is to use the 7th edition (see Appendix A).

8 SNOMED coding

See Appendix B.

9 Reporting of small biopsy specimens

In specialist ocular oncology centres, aspiration cytology (iris, ciliary body and choroid – the latter via a trans-vitreous approach) and open-flap biopsies are undertaken to usually distinguish between a uveal melanoma, metastasis or benign neoplasm, prior to treatment. Aspiration cytology specimens are handled as cytopsins and cell blocks. These preparations often yield enough material for immunohistochemistry and molecular prognostication testing. The iris and choroid are amenable to direct biopsy. These specimens are small and require careful handling so that ancillary investigations, such as immunohistochemistry and molecular studies are possible, to secure a firm diagnosis/prognosis.

10 Reporting of frozen sections

Not applicable.

11 Specific aspects of individual tumours not covered elsewhere

11.1 Molecular testing^{38–42}

Loss of chromosome 1p, monosomy 3, gain of 6p, loss of 6q, loss of 8p and gain of 8q have been linked statistically to metastatic death in uveal melanoma, of which monosomy 3 is at present the most significant. There are a variety of molecular and cytogenetic prognostic tests available (karyotyping, fluorescence in-situ hybridisation, comparative genomic hybridisation, microsatellite analysis, single-nucleotide polymorphism, multiplex ligation-dependent probe amplification, uveal melanoma gene expression profiling). Whilst this dataset relates to histopathological prognostic factors, it is highly recommended that pathologists reporting ciliary body and choroidal melanomas have access to some form of molecular or cytogenetic testing and, *as a minimum*, communicate the status of chromosome 3. Increasingly molecular testing is being asked for prognostication and treatment prediction purposes, and hence these samples must be worked up sparingly, allowing for DNA extraction from a portion of them.

11.2 Iris cytology^{43,44}

Care is required when interpreting surface aspiration cytology specimens of suspected melanoma of the iris. It is now thought that aqueous humour induces iris melanoma cells to adopt low-grade cytology which resemble naevus cells. Finding such cells in an aspiration specimen does not exclude melanoma. In such circumstances, a formal iris biopsy is required to sample the deeper stromal melanoma cells, and to allow for interpretation of any atypical cells in relation to the iris architecture. These deeper cells are usually more atypical and permit a secure diagnosis of melanoma to be made.

12 Criteria for audit of the dataset

As recommended by the RCPATH as key performance indicators (see *Key Performance Indicators – Proposals for implementation*, www.rcpath.org/clinical-effectiveness/kpi/KPI, July 2013), the criteria for audit are as follows.

- 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.

Whilst no standards exist for the following, it is suggested that it would be beneficial to monitor:

- the proportion of cases in each 'T' category (pTNM) and prognosis
- the proportions of spindle, mixed and epithelioid tumours, and associated prognosis. When reporting epithelioid cell tumours, it would be useful to estimate the epithelioid cell component. In this way, consensus may be achieved as to what constitutes a 'mixed' tumour.

13 References

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Appendix A TNM pathological staging of uveal melanoma (TNM 7th edition)¹

Anatomical sites

Iris	C69.4
Ciliary body	C69.4
Choroid	C69.3

pT – Primary tumour

pTX	Primary tumour cannot be assessed
pT0	No evidence of primary tumour

Iris

Note: Iris melanomas originate from, and are predominantly located in, this region of the uvea. If less than half of the tumour volume is located within the iris, the tumour may have originated in the ciliary body and consideration should be given to classifying it accordingly.

pT1:	Tumour limited to the iris
pT1a:	Not more than 3 clock hours in size
pT1b:	More than 3 clock hours in size
pT1c:	With secondary glaucoma
pT2:	Tumour confluent with or extending into the ciliary body, choroid or both
pT2a:	With secondary glaucoma
pT3:	Tumour confluent with or extending into the ciliary body, choroid or both, with scleral extension
pT3a:	With secondary glaucoma
pT4:	Tumour with extrascleral extension
pT4a:	≤5 mm in diameter
pT4b:	>5 mm in diameter.

Ciliary body and choroid

Primary ciliary body and choroidal melanomas are classified according to the four tumour size categories shown in the table below.

Thickness (mm)

>15					4	4	4
12.1–15.0				3	3	4	4
9.1–12.0		3	3	3	3	3	4
6.1–9.0	2	2	2	2	3	3	4
3.1–6.0	1	1	1	2	2	3	4
≤3.0	1	1	1	1	2	2	4
	<3.0	3.1–6.0	6.1–9.0	9.1–12.0	12.1–15.0	15.1–18.0	>18

Largest basal diameter of tumour (mm)

pT1 Tumour size category 1

pT1a Without ciliary body involvement and extraocular extension

pT1b Without ciliary body involvement

pT1c Without ciliary body involvement but with extraocular extension ≤5 mm in diameter

pT1d With ciliary body involvement and extraocular extension ≤5 mm in diameter

pT2 Tumour size category 2

pT2a Without ciliary body involvement and extraocular extension

pT2b With ciliary body involvement

pT2c Without ciliary body involvement

pT2d With ciliary body involvement and extraocular extension ≤5 mm in diameter

pT3 Tumour size category 3

T3a Without ciliary body involvement and extraocular extension

T3b With ciliary body involvement

T3c Without ciliary body involvement but with extraocular extension ≤5 mm in diameter

T3d With ciliary body involvement and extraocular extension ≤5 mm in diameter

pT4 Tumour size category 4

pT4a Without ciliary body involvement and extraocular extension

pT4b With ciliary body involvement

pT4c Without ciliary body involvement but with extraocular extension ≤5 mm in diameter

pT4d With ciliary body involvement and extraocular extension ≤5 mm in diameter

pT4e Any tumour size category with extraocular extension ≥5 mm in diameter

Note: When histopathological measurements are recorded after fixation, tumour diameter and thickness may be underestimated because of tissue shrinkage.

pN – Regional lymph nodes

The regional lymph nodes are the preauricular, submandibular and cervical nodes.

pNX Regional lymph nodes cannot be assessed

pN0 No regional lymph node metastasis

pN1 Regional lymph node metastasis

pM – Distant metastasis

M0 No distant metastasis

pM1 Distant metastasis

pM1a Largest diameter of the largest metastasis 3 cm or less

pM1b Largest diameter of the largest metastasis 3.1–8.0 cm

pM1c Largest diameter of the largest metastasis 8 cm or more

Appendix B SNOMED codes

SNOMED T codes

Topographical codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Eye	TXX000 (SNOMED 2) TAA000 (SNOMED 3/RT)	Structure of eye proper (body structure)	81745001
Both eyes	TXX180 (SNOMED 2) TAA180 (SNOMED 3/RT)	Structure of both eyes (body structure)	40638003
Orbit	TY0480 (SNOMED 2) TD1480 (SNOMED 3) T-D14AD (SNOMED RT)	Entire orbital region (body structure)	39607008
Choroid	T-XX310 (SNOMED 2) T-AA310 (SNOMED 3/RT)	Choroidal structure (body structure)	68703001
Ciliary body	T-XX400 (SNOMED 2) T-AA400 (SNOMED 3/RT)	Ciliary body structure (body structure)	29534007
Iris	T-XX280 (SNOMED 2) T-AA500 (SNOMED 3/RT)	Iris structure (body structure)	41296002
Uvea	T-XX570 (SNOMED 2) T-AA570 (SNOMED 3/RT)	Uveal tract structure (body structure)	74862005

SNOMED M codes

Morphological codes	SNOMED	SNOMED CT terminology	SNOMED CT code
Melanoma	M-87203	Malignant melanoma, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	2092003
Epithelioid melanoma	M-87713	Epithelioid cell melanoma (morphologic abnormality)	37138001
Spindle cell melanoma	M-87723	Spindle cell melanoma (morphologic abnormality)	68827007
Mixed spindle cell and epithelioid melanoma	M-87703	Mixed epithelioid and spindle cell melanoma (morphologic abnormality)	50813003

Morphological codes (continued)	SNOMED	SNOMED CT terminology	SNOMED CT code
Melanoma in melanosis	M-87413	Malignant melanoma in precancerous melanosis (morphologic abnormality)	18450009
Naevus	M-87200	Pigmented nevus, no International Classification of Diseases for Oncology subtype (morphologic abnormality)	21119008
Melanocytoma	M-87260	Magnocellular nevus (morphologic abnormality)	26325004
Metastatic melanoma	M-87206	Malignant melanoma, metastatic (morphologic abnormality)	372158004

SNOMED P (Procedure) codes

These are used in SNOMED 2 and SNOMED 3 to distinguish biopsies, partial resections and radical resections to indicate the nature of the procedure.

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

Appendix C Reporting proforma for uveal melanoma

Surname: Forenames: Date of birth: Sex: M / F
Hospital: Hospital no: NHS/CHI number:
Date specimen taken: Date of receipt: Date of reporting:
Report no: Pathologist: Surgeon:

MACROSCOPIC DESCRIPTION

Specimen type: Iridectomy Local resection of ciliary body/choroid
Endo-resection Enucleation Orbital exenteration

Laterality: Right Left

Uveal structures involved: Iris Ciliary body Choroid Cannot be assessed

Extraocular tumour extension: Present Not identified

If extraocular extension present:
Extraocular extension maximum tumour diameter: ≤5 mm >5 mm Cannot be assessed

Intraocular tumour size (for choroidal and ciliary body tumours only):
Largest basal diameter (mm):
≤3.0 3.1–6.0 6.1–9.0 9.1–12.0 12.1–15.0 15.1–18.0 >18
Maximum height (mm):
≤3.0 3.1–6.0 6.1–9.0 9.1–12.0 12.1–15.0 >15

MICROSCOPIC DESCRIPTION

Melanoma present Yes No

Uveal structures involved: Iris Ciliary body Choroid Cannot be assessed

Tumour growth pattern: Focal solid mass Ring Diffuse

Histological tumour type:
Spindle cell melanoma (>90% spindle cells)
Mixed cell melanoma (>10% epithelioid cells and <90% spindle cells)
Epithelioid cell melanoma (>90% epithelioid cells)
Other Please specify

Microscopic extraocular extension: Present Not identified

If microscopic extraocular extension present:

Microscopic extraocular extension maximum tumour diameter:

≤5 mm >5 mm Cannot be assessed

**Presence of extracellular matrix networks and loops
(for ciliary body and choroid melanoma only)**

Present Not identified

Additional comments:

Pathological staging (y)pT (y)pN (y)pM (TNM 7th edition)

SNOMED codes T...../ M.....

Signature..... **Date**.....

Appendix D

Proforma in list format

Element name	Values	Implementation notes
Specimen type	Single selection value list: <ul style="list-style-type: none"> • Iridectomy • Local resection of ciliary body/choroid • Endo-resection • Enucleation • Orbital exenteration 	
Laterality	Single selection value list: <ul style="list-style-type: none"> • Left • Right 	
Macroscopic uveal structures involved	Multi select value list (choose all that apply): <ul style="list-style-type: none"> • Iris • Ciliary body • Choroid • Cannot be assessed 	
Macroscopic extraocular tumour extension	Single selection value list: <ul style="list-style-type: none"> • Present • Not identified 	
Macroscopic extraocular tumour extension maximum tumour diameter	Single selection value list: <ul style="list-style-type: none"> • ≤5 mm • >5 mm • Cannot be assessed • Not applicable 	Not applicable if macroscopic extraocular tumour extension is not identified.
Largest basal diameter	Single selection value list: <ul style="list-style-type: none"> • ≤3.0 • 3.1–6.0 • 6.1–9.0 • 9.1–12.0 • 12.1–15.0 • 15.1–18.0 • >18 • Not applicable 	Not applicable if uveal compartments involved does not include ciliary body or choroid.
Maximum height	Single selection value list: <ul style="list-style-type: none"> • ≤3.0 • 3.1–6.0 • 6.1–9.0 • 9.1–12.0 • 12.1–15.0 • >15 • Not applicable 	Not applicable if uveal compartments involved does not include ciliary body or choroid.
Melanoma present	Single selection value list: <ul style="list-style-type: none"> • Yes • No 	

Microscopic uveal structures involved	Multi select value list (choose all that apply): <ul style="list-style-type: none"> • Iris • Ciliary body • Choroid • Cannot be assessed 	
Histological tumour type	Single selection value list: <ul style="list-style-type: none"> • Spindle cell melanoma • Mixed cell melanoma • Epithelioid cell melanoma • Other 	
Histological tumour type, other specify	Free text	Only applicable if 'Histological tumour type, other' selected.
Microscopic extraocular tumour extension	Single selection value list: <ul style="list-style-type: none"> • Present • Not identified 	
Microscopic extraocular tumour extension maximum tumour diameter	Single selection value list: <ul style="list-style-type: none"> • ≤ 5 mm • >5 mm • Cannot be assessed • Not applicable 	Not applicable if microscopic extraocular tumour extension is not identified.
Presence of extracellular matrix networks and loops	Single selection value list: <ul style="list-style-type: none"> • Present • Not identified • Not applicable 	Not applicable if uveal compartments involved does not include ciliary body or choroid
UICC TNM version 7 pT stage	Single selection value list: <ul style="list-style-type: none"> • pTX • pT0 • pT1a • pT1b • pT1c • pT1d • pT2a • pT2b • pT2c • pT2d • pT3a • pT3b • pT3c • pT3d • pT4a • pT4b • pT4c • pT4d • pT4e • ypTX • ypT0 	

	<ul style="list-style-type: none"> • ypT1a • ypT1b • ypT1c • ypT1d • ypT2a • ypT2b • ypT2c • ypT2d • ypT3a • ypT3b • ypT3c • ypT3d • ypT4a • ypT4b • ypT4c • ypT4d • ypT4e 	
UICC TNM version 7 pN stage	<p>Single selection value list:</p> <ul style="list-style-type: none"> • pNX • pN0 • pN1 • ypNX • ypN0 • ypN1 	
UICC TNM version 7 pM stage	<p>Single selection value list:</p> <ul style="list-style-type: none"> • M0 • pM1a • pM1b • pM1c 	
SNOMED Topography code	<p>May have multiple codes. Look up from SNOMED tables</p>	
SNOMED Morphology code	<p>May have multiple codes. Look up from SNOMED tables</p>	

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	<p>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</p> <p>or</p> <p>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.</p>
Level B	<p>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</p> <p>or</p> <p>Extrapolation evidence from studies described in A.</p>
Level C	<p>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</p> <p>or</p> <p>Extrapolation evidence from studies described in B.</p>
Level D	<p>Non-analytic studies such as case reports, case series or expert opinion</p> <p>or</p> <p>Extrapolation evidence from studies described in C.</p>
Good practice point (GPP)	<p>Recommended best practice based on the clinical experience of the authors of the writing group.</p>

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	Foreword, 1
Stakeholder involvement	
4 The guideline development group includes individuals from all the relevant professional groups	Foreword
5 The patients' views and preferences have been sought	n/a *
6 The target users of the guideline are clearly defined	1
7 The guideline has been piloted among target users	Feedback from previous edition
Rigour of development	
8 Systematic methods were used to search for evidence	Foreword
9 The criteria for selecting the evidence are clearly described	Foreword
10 The methods used for formulating the recommendations are clearly described	1
11 The health benefits, side effects and risks have been considered in formulating the recommendations	1
12 There is an explicit link between the recommendations and the supporting evidence	3–6, 11
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 are clearly presented	2–11
17 Key recommendations are easily identifiable	2–11
18 The guideline is supported with tools for application	Appendices A–C
Applicability	
19 The potential organisational barriers in applying the recommendations have been discussed	Foreword
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 the Director of Communications 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.