UICC

TNM Classification of Malignant Tumours

9th Edition

Edited by: James Brierley,
Meredith Giuliani, Brian O'Sullivan,
Brian Rous, Elizabeth Van Eycken

WILEY

TNM
Classification of Malignant Tumours

Union for International Cancer Control (UICC)

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Ninth Edition

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They are called wise
who put things in their right order
Thomas Aquinas

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Preface

In this ninth edition of the *TNM Classification of Malignant Tumours*, many of the tumour sites are unchanged from the eighth edition.[1] However, some tumour entities and anatomic sites have been newly introduced and some tumours contain modifications: this follows the basic philosophy of maintaining stability of the classification over time. The modifications and additions reflect new data on prognosis as well as new methods for assessing prognosis.[2] Some changes had already appeared in the *TNM Supplement*[3] as proposals. Subsequent support warrants their incorporation into the classification.

In the seventh edition, a new approach was adopted to separate stage groupings from prognostic groupings in which other prognostic factors are added to T, N and M categories. These new prognostic groupings were presented for oesophagus and prostate. In this ninth edition, as in the eighth edition, the term 'stage' is used when only descriptions of anatomic extent of disease are used and 'prognostic group' is used when additional prognostic factors are incorporated.

Changes made between the eighth and ninth editions are indicated by a bar at the left-hand side of the text. To avoid ambiguity, users are encouraged to cite the edition and year of the TNM publication they have used in their list of references.

A TNM web page with Frequently Asked Questions (FAQs) and a form for submitting questions or comments on the TNM can be found at: http://www.uicc.org. Readers are also encouraged to visit http://www.uicc.org for updates and errata. Evidence-based proposals for changes can be submitted for assessment. More details and a checklist that will facilitate the formulation of proposals can be obtained at http://www.uicc.org.

The AJCC is no longer publishing a Manual alongside this ninth edition of *TNM Classification of Malignant Tumours*, instead it will publish a series of rolling updates. In line with FIGO and the corresponding UICC update available at http://www.uicc.org, it started with carcinoma of the cervix in 2021.

As with carcinoma of the cervix, changes in this ninth edition result from consultations between the UICC TNM project, the AJCC and other expert groups such as FIGO and IASLC for thoracic tumours, and other global tumour groups, consortia and national TNM committees.

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The ninth edition of the *TNM Classification* is the result of a number of consultative meetings organised and supported by the UICC and AJCC secretariats, with particular thanks to Zuzanna Tittenbrun.

Organisations Associated with the TNM System

CDC	Centers for Disease Control and Prevention (USA)
FIGO	International Federation of Gynaecology and Obstetrics
IACR	International Association of Cancer Registries
IARC	International Agency for Research on Cancer
IASLC	International Association for the Study of Lung Cancer
ICCR	International Collaboration on Cancer Reporting
WHO	World Health Organization

Members of UICC Committees Associated with the TNM System

In 1950, the UICC appointed a *Committee on Tumour Nomenclature and Statistics*. In 1954, this Committee became known as the *Committee on Clinical Stage Classification and Applied Statistics*, and, in 1966, it was named the *Committee on TNM Classification*. Taking into consideration new prognostic factors the Committee was named in 1994 the *TNM Prognostic Factors Project Committee*, and in 2003 the main committee was named 'TNM Prognostic Factors Core Group'. A list of members who have served on these committees is available at: www.uicc.org

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Global Advisory Group Members	See www.uicc.org

Introduction

The History of the TNM System*

The TNM system for the classification of malignant tumours was developed by Pierre Denoix (France) between the years 1943 and 1952.[1]

In 1950, the UICC appointed a Committee on Tumour Nomenclature and Statistics. As a basis for its work on clinical stage classification, it adopted the general definitions of local extension of malignant tumours suggested by the World Health Organization (WHO) Sub-Committee on The Registration of Cases of Cancer as well as Their Statistical Presentation.[2]

In 1958, the Committee published the first recommendations for the clinical stage classification of cancers of the breast and larynx and for the presentation of results.[3]

A second publication in 1959 presented revised proposals for the breast, for clinical use and evaluation over a 5-year period (1960–1964).[4] In 1968, a booklet, the *Livre de Poche*,[5] and, a year later, a complementary booklet were published detailing recommendations for the setting-up of field trials, for the presentation of end results, and for the determination and expression of cancer survival rates.[6] The *Livre de Poche* was subsequently translated into 11 languages. In 1974 and 1978, second and third editions[7,8] were published containing new site classifications, and the fourth edition of TNM was published in 1987.[9]

In 1993, the project published the *TNM Supplement*[10] to promote the uniform use of TNM by providing detailed explanations of the TNM rules with practical examples. Second, third, fourth and fifth editions appeared in 2001, 2003, 2012 and 2019, respectively.[11–14]

The project also publishes the *TNM Atlas: Illustrated Guide to the TNM Classification of Malignant Tumours*; the seventh edition was published in 2021 as a companion to the eighth edition of the *TNM Classification*.[15]

In 1995, the project published *Prognostic Factors in Cancer*,[16] a compilation and discussion of prognostic factors in cancer, both anatomical and non-anatomical, at each of the body sites. This was expanded in the second edition in 2001[17] and the third edition in 2006.[18]

The current ninth edition of TNM contains rules of classification and staging that correspond with those appearing in the eighth edition of the *AJCC Cancer Staging Manual* (2017) and subsequent version 9 series.[19,20] While the aim of the UICC and AJCC is to have identical classifications, small differences exist and are identified as footnotes to the text. Wherever possible, the classifications are

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based on published evidence-based recommendation and analysis of databases that reflect contemporary management.

To develop and sustain a classification system acceptable to all requires the closest liaison between national and international organisations. As noted, while the classification is based on published evidence, in areas where high-level evidence is not available, it is based on international consensus. The continuing objective of the UICC is to present the classification of anatomical extent of cancer for global use in high-, middle- and low-income countries.

Note

* A more detailed history is available on the website at www.uicc.org.

The Principles of the TNM System

The determination of the extent of any malignancy is a prerequisite to determine both prognosis and appropriate treatment for any patient with cancer. The practice of classifying cancer cases into groups according to anatomical extent, termed 'stage', arose from the observation that survival rates were higher for cases in which the disease was localised than for those in which the disease had extended beyond the organ of origin. The stage of disease at the time of diagnosis is a reflection of not only the rate of growth and extension of the neoplasm but also the type of tumour and the tumour–host relationship.

It is important to record accurate information on the anatomical extent of the disease for each site at the time of diagnosis, to meet the following objectives:

1. to aid the clinician in the planning of treatment
2. to give some indication of prognosis for survival
3. to assist in the evaluation of the results of treatment
4. to facilitate the exchange of information between treatment centres and regions
5. to contribute to the continuing investigation of human cancer
6. to support cancer control activities.

Cancer staging is essential to patient care, research and cancer control. Cancer control activities include direct patient-care-related activities, the development and implementation of clinical practice guidelines and centralised activities such as recording disease extent in cancer registries for surveillance purposes and planning cancer systems. Recording of stage is essential for the evaluation of outcomes of clinical practice and cancer programmes, including screening. However, in order to evaluate the long-term outcomes of populations, it is ideal if the classification remains stable. There is therefore a conflict between a classification that is updated to include the most current forms of medical knowledge and a classification that facilitates longitudinal studies. The UICC TNM Project aims to address both needs.

International agreement on the classification of cancer by the extent of disease provides a method of conveying disease extent to others without ambiguity.

There are many axes of tumour classification: for example, the anatomical site and the clinical and pathological extent of disease, the duration of symptoms or signs,

the gender, age, comorbidities and performance status of the patient, and the histological type and grade of the tumour and relevant molecular and genetic markers. All of these have an influence on the outcome of the disease and need to be considered in tailoring the treatment for an individual patient. Classification by the anatomical extent of disease is the one with which the UICC TNM system primarily deals.

The clinician's immediate task when meeting a patient with a new diagnosis of cancer is to make a judgement as to prognosis and decide on the most effective course of treatment. This judgement and decision require, among other things, an objective assessment of the anatomical extent of the disease.

The General Rules of the TNM System*

The TNM system for describing the anatomical extent of disease is based on the assessment of three components:

T – the extent of the primary tumour
N – the absence or presence and extent of regional lymph node metastasis
M – the absence or presence, extent and the site of distant metastasis

The addition of Arabic numerals determines the categories for each of these three components, which indicate the extent of the malignant disease:

T0, T1, T2, T3, T4, N0, N1, N2, N3, M0, M1

In effect, the system is a 'shorthand notation' for describing the extent of a particular malignant tumour.

The general rules applicable to all sites are as follows:

1. All cases should be confirmed microscopically. Any cases not so proved must be analysed and reported separately.
   Two classifications are described for each site.
   a) *Clinical classification*: the pre-treatment clinical classification, designated **cTNM**, is essential to select and evaluate therapy. This is based on evidence acquired before any treatment. Such evidence is gathered from physical examination, imaging, endoscopy, biopsy, surgical exploration and other relevant examinations.
   b) *Pathological classification*: the postsurgical histopathological classification, designated **pTNM**, is based on evidence acquired before treatment, supplemented or modified by additional evidence acquired from surgery and from pathological examination. It is used to provide additional data to estimate prognosis and assessment for any additional treatment. The pathological assessment of the primary tumour (pT) entails resection of the primary tumour or biopsy adequate to confirm the highest pT category. Following two surgical procedures for a single lesion, the pTNM classification should be a composite of the histological examination of the specimens from both operations.

2. The pathological assessment of regional lymph nodes requires examination of at least one lymph node and the pathological assessment of the primary tumour (pT), except in cases of unknown primary (T0). If a biopsy confirms the highest N category, the use of pN is appropriate. An excisional biopsy of a lymph node without pathological assessment of the primary tumour (pT) is insufficient to fully evaluate the pN category and is a clinical N category and stage, except in the case of an unknown primary (T0). The pathological assessment of distant metastasis (pM) entails microscopic examination of metastatic deposit. However, if both the highest T and N categories or the M1 category are confirmed microscopically including biopsy without removal of the primary, the criteria for pathological staging are considered satisfied.
3. After assigning cT, cN and cM and/or pT, pN and pM categories, these may be grouped into stages, which are designated by Roman numerals.
   The TNM classification and stages, once established, must remain unchanged in the medical records. For cancer surveillance purposes, clinical and pathological data may be combined when only partial information is available in either the pathological classification or the clinical classification; this should be noted. How stage grouping is determined should be recorded.
4. If there is doubt concerning the correct T, N, or M category to which a particular case should be allotted, then the lower (i.e., less advanced) category should be chosen. This will also be reflected in the stage; however, the treating physician may recommend treatment as for the higher stage. This rule does not apply to situations where there is insufficient information to stage, where TX or NX should be used, nor does this rule apply to cancer registries interpreting apparently conflicting information.
5. In the case of multiple primary tumours in one organ of the same histology, the tumour with the highest T category should be classified and the multiplicity or the number of tumours should be indicated in parentheses, e.g., T2(m) or T2(5). In simultaneous bilateral primary cancers of paired organs, each tumour should be classified independently. Exceptions include tumours where bilaterality or multiplicity is a component of the T or M category definitions and in malignant melanoma for which, when patients present with multiple primaries, each anatomical skin site is considered a different primary and should be classified separately.
6. Definitions of the TNM categories and stage may be telescoped or expanded for clinical or research purposes as long as the basic definitions recommended are not changed. For instance, any T, N, or M can be divided into subcategories, such as T1a and T1b.
7. Previously the UICC did not specify a specific time frame within which staging information should be obtained. The AJCC recommends that staging should be complete within 4 months of the original diagnosis. Exceptionally, the presence of metastases may be confirmed after 4 months from diagnosis, and if the treating physician is of the opinion that they were present but unconfirmed at diagnosis, that data may be used; otherwise, staging should be complete within 4 months of original diagnosis and remain unchanged.

Note

* An educational module on the general principles is available on the UICC website at www.uicc.org.

Anatomical Regions and Sites

The sites in this classification are listed by code number of the International Classification of Diseases for Oncology.[21] Each region or site is described under the following headings:

- Anatomical sites, and subsites if appropriate
- Definition of the regional lymph nodes
- cTNM clinical classification
- pTNM pathological classification
- G histopathological grading if different from that described on page 8
- Stage and prognostic groups
- Prognostic factors grid

cTNM Clinical Classification

The following general definitions are used throughout:

cT – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cT1–T4	Increasing size* and/or local extent of the primary tumour

Note

* The UICC does not prescribe the way to measure tumour size for pT classification; however, the AJCC Cancer Staging Manual 2017 [19] recommends that pT is derived from the actual measurement of the unfixed tumour in the surgical specimen. It should be noted, however, that up to 30% shrinkage of soft tissues may occur in the resected specimen. Thus, in cases of discrepancies of clinically and pathologically measured tumour size, the clinical measurement should also be considered for the pT classification.

N – Regional Lymph Nodes

cNX	Regional lymph nodes cannot be assessed
cN0	No regional lymph node metastasis
cN1–N3	Increasing involvement of regional lymph nodes

M – Distant Metastasis*

cM0	No distant metastasis
cM1	Distant metastasis

Note

* The MX category is considered to be inappropriate as clinical assessment of metastasis can be based on physical examination alone. (The use of MX may result in exclusion from staging.)

The category M1 may be further specified according to the following notation:

Pulmonary	PUL (C34)	Bone marrow	MAR (C42.1)
Osseous	OSS (C40, 41)	Pleura	PLE (C38.4)
Hepatic	HEP (C22)	Peritoneum	PER (C48.1,2)
Brain	BRA (C71)	Adrenals	ADR (C74)
Lymph nodes	LYM (C77)	Skin	SKI (C44)
Others	OTH		

Subdivisions of TNM

Subdivisions of some main categories are available for those who need greater specificity (e.g., cT1a, cT1b or cN2a, cN2b).

pTNM Pathological Classification

The following general definitions are used throughout:

pT – Primary Tumour

pTX	Primary tumour cannot be assessed histologically
pT0	No histological evidence of primary tumour
pTis	Carcinoma in situ
pT1–4	Increasing size and/or local extent of the primary tumour histologically

pN – Regional Lymph Nodes

pNX	Regional lymph nodes cannot be assessed histologically
pN0	No regional lymph node metastasis histologically
pN1–N3	Increasing involvement of regional lymph nodes histologically

Notes

- Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis.
- Tumour deposits (TD) represent discrete tumour nodules of any shape, contour or size in peri-rectal and peri-colonic fat, away from the leading edge of the tumour, within the lymph drainage area of the primary carcinoma. TD can originate from different histological structures, including lymph nodes, vessels and nerves. Therefore, TD may contain foci of extramural vascular invasion (EMVI) and perineural invasion (PNI). The feature distinguishing a TD from EMVI and PNI is the presence of unequivocal tumour extension from the vessel or nerve into the surrounding fat or fibroconnective tissue.
- When tumour outgrowth from EMVI and/or PNI is present, the diagnosis of TD and EMVI/PNI should be denoted separately in the report. If the tumour involves an identifiable lymph node, it is considered as lymph node metastasis and not as tumour deposit even if the tumour extends into the perinodal fat.
- Metastasis in any lymph node other than regional is classified as a distant metastasis.

- When size is a criterion for pN classification, measurement is made of the metastasis within the node, not of the entire lymph node. The measurement should be that of the largest dimension of the tumour.
- Cases with micrometastasis only, i.e., no metastasis larger than 2 mm, can be identified by the addition of '(mi)', e.g., pN1(mi).

Sentinel Lymph Node

The sentinel lymph node is the first lymph node to receive lymphatic drainage from a primary tumour. If it contains metastatic tumour, this indicates that other lymph nodes may contain tumour. If it does not contain metastatic tumour, other lymph nodes are not likely to contain tumour. Occasionally, there is more than one sentinel lymph node.

The following designations are applicable when sentinel lymph node assessment is attempted:

(p)N0(sn) No sentinel lymph node metastasis
(p)N1(sn) Sentinel lymph node metastasis

Isolated Tumour Cells

Isolated tumour cells (ITCs) are single tumour cells or small clusters of cells not more than 0.2 mm in greatest extent that can be detected by routine H and E stains or immunohistochemistry [22]. An additional criterion has been proposed in breast cancer to include a cluster of fewer than 200 cells in a single histological cross-section. Definitions of ITCs may vary by tumour site. ITCs do not typically show evidence of metastatic activity (e.g., proliferation or stromal reaction) or penetration of vascular or lymphatic sinus walls. Cases with ITCs in lymph nodes should be classified as N0. The same applies to cases with findings suggestive of tumour cells or their components by non-morphological techniques such as flow cytometry or DNA analysis. The exceptions are in malignant melanoma of the skin and Merkel cell carcinoma, wherein ITCs in a lymph node are classified as N1a (clinically occult) or N2a. These cases should be analysed separately.[20] Their classification is as follows:

N0	No regional lymph node metastasis histologically, no examination for isolated tumour cells (ITC)
N0(i–)	No regional lymph node metastasis histologically, negative morphological findings for ITC
N0(i+)	No regional lymph node metastasis histologically, positive morphological findings for ITC
N0(mol–)	No regional lymph node metastasis histologically, negative non-morphological findings for ITC
N0(mol+)	No regional lymph node metastasis histologically, positive non-morphological findings for ITC

Cases with or examined for ITCs in sentinel lymph nodes can be classified as follows:

N0(i–)(sn)	No sentinel lymph node metastasis histologically, negative morphological findings for ITC
N0(i+)(sn)	No sentinel lymph node metastasis histologically, positive morphological findings for ITC
N0(mol–)(sn)	No sentinel lymph node metastasis histologically, negative non-morphological findings for ITC
N0 (mol+)(sn)	No sentinel lymph node metastasis histologically, positive non-morphological findings for ITC

pM – Distant Metastasis*

pM1 Distant metastasis microscopically confirmed

Note

* pM0 and pMX are not valid categories.

The category pM1 may be further specified in the same way as M1 (see page 5).

ITCs found in bone marrow and circulating tumour cells with morphological techniques are classified according to the scheme for N, e.g., M0(i+). For non-morphological findings, 'mol' is used in addition to M0, e.g., M0 (mol+).

Circulating tumour DNA in the absence of established metastases is also classified as M0; to date, there is no identifying suffix for circulating tumour DNA.

Histopathological Grading

In most sites, further information regarding the primary tumour may be recorded under the following heading:

G – Histopathological Grading

GX Grade of differentiation cannot be assessed
G1 Well differentiated
G2 Moderately differentiated
G3 Poorly differentiated
G4 Undifferentiated

Notes

- In some tumour sites, Grades 3 and 4 can be combined as 'G3, poorly differentiated or undifferentiated'.
- In some tumour sites, tumours may be classified as low or high grade.
- Occasionally, special systems of grading are recommended, for example, prostate adenocarcinoma.

Additional Descriptors

For identification of special cases in the TNM or pTNM classification, the m, y, r and a symbols may be used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

m Symbol. The suffix m, in parentheses, is used to indicate the presence of multiple primary tumours at a single site. See TNM rule no. 5 (page 4).

y Symbol. In those cases in which classification is performed during or following multimodality therapy, the cTNM or pTNM category is identified by a y prefix. The ycTNM or ypTNM categorises the extent of tumour actually present at the time of that examination. The y categorisation is not an estimate of the extent of tumour prior to multimodality therapy. Only viable tumour cells and not signs of regressed tumour tissue such as necrotic cell debris, scars, fibrotic areas, fibrotic nodules, granulation tissue, mucin lakes, etc., should be considered when assigning the yp categories.

r Symbol. Recurrent tumours, when classified after a disease-free interval, are identified by the prefix r. It may also be used for progression after watchful waiting.

a Symbol. The prefix a indicates that classification is first determined at autopsy.

Optional Descriptors

L – Lymphatic Invasion

LX Lymphatic invasion cannot be assessed
L0 No lymphatic invasion
L1 Lymphatic invasion

V – Venous Invasion

VX Venous invasion cannot be assessed
V0 No venous invasion
V1 Microscopic venous invasion
V2 Macroscopic venous invasion

LV – Lymphovascular Invasion

LVX Lymphovascular invasion cannot be assessed
LV0 No lymphovascular invasion
LV1 Lymphovascular invasion

Note
Macroscopic involvement of the wall of veins (with no tumour within the veins) is classified as V2.

Pn – Perineural Invasion

PnX Perineural invasion cannot be assessed
Pn0 No perineural invasion
Pn1 Perineural invasion

In some tumour sites, perineural invasion may be incorporated into the definition of the T category.

Residual Tumour (R) Classification[a,b]

The absence or presence of residual tumour after treatment is described by the symbol R.

cTNM and pTNM describe the anatomical extent of cancer in general without considering treatment. They can be supplemented by the R classification, which deals with tumour status after treatment. It reflects the effects of therapy, including surgical extent, and is a predictor of prognosis.

The definitions of the R categories are:

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

Notes

[a] Many consider the R classification to apply only to the primary tumour and its local or regional extent. Others have applied it more broadly to include distant metastasis. Detailed definitions of R1 used can vary by tumour type; therefore, the specific usage should be indicated.

[b] After neoadjuvant therapy for certain tumour types, pathological classifications of the extent of the residual disease exist, such as the tumour regression score for rectal cancer and oesophageal cancer and residual cancer burden in breast cancer may be used. Classifications vary by tumour type and there is not as yet universal consensus on definitions.

Unknown Primary

In the absence of a primary tumour, when the origin is histologically identified, such as breast lobular carcinoma, but there is no evidence of a primary tumour, the T category can be coded as T0. The assessments of the N and M categories can be coded as appropriate.

Specifically in the head and neck section, there is a subsection on unknown primary with cervical lymph nodes that assumes that the primary tumour is located somewhere in the head and neck region; see page 44.

If there is evidence of HPV positivity or EB virus positivity, the node is staged as if the primary is from the oropharynx or nasopharynx, respectively.

Staging of Tumours for Which No TNM Classification Is Provided

Staging according to the rules of the SEER Program may be used if no TNM classification is provided (see website link: https://training.seer.cancer.gov/staging/systems/summary.html).

Note may be made of whether the tumour is local, regional, or distant.

Stage and Prognostic Groups

The TNM system is used to describe and record the anatomical extent of disease. For purposes of tabulation and analysis, it is useful to condense these categories into groups. For consistency, in the TNM system, carcinoma in situ is categorised stage 0; in general, tumours localised to the organ of origin as stages I and II, locally extensive spread, particularly to regional lymph nodes as stage III, and those with distant metastasis as stage IV. The stage adopted is such as to ensure, as far as possible, that each group is more or less homogeneous in respect of survival and that the survival rates of these groups for each cancer site are distinctive.

For pathological stages, both pT and pN categories must be assigned unless there is microscopic confirmation of metastasis (pM1). In the absence of pM1, if either the T category is cT or the N category is cN, then a clinical stage is assigned. If both pT and pN categories are assigned, the M category may be clinical (cM) or pathological (pM) for assigning a pathological stage. If the pT category is based on biopsy confirming the highest T category, there must also be microscopic evidence confirming the highest N category to assign a pathological stage; otherwise, the stage is clinical if sufficient tissue has been removed for pathological examination to evaluate the highest T and N categories.

Although the anatomical extent of disease, as categorised by TNM, is a very powerful prognostic indicator in cancer, it is recognised that many factors have a significant impact on predicting outcomes. This has resulted in different stage groups. In thyroid cancer, there are different stage definitions for different histologies and in oropharyngeal cancer. HPV-associated cancer is staged differently from HPV-independent cancer. Some factors have been combined with TNM in the development of stage groupings; for instance, for different histologies (thyroid), different major prognostic factor groups (age in thyroid) and by aetiology (HPV-independent oropharyngeal cancer). In this edition, the term **stage** has been used as defining the anatomical extent of disease while **prognostic group** for classifications that incorporate other prognostic factors such as in oesophageal cancer. Historically, age in differentiated thyroid cancer and grade in soft tissue sarcoma are combined with the anatomical extent of disease to determine the stage, and the stage is retained rather than the prognostic group in these two sites.

Prognostic Factors Classification

Prognostic factors can be classified as those pertaining to:

- **Anatomic extent of disease** describes the extent of disease in the patient at the time of diagnosis. Classically, this is TNM but may also include tumour markers that reflect tumour burden, for instance, prostate-specific antigen (PSA) in prostate carcinoma or carcinoembryonic antigen (CEA) in colorectal carcinoma.
- **Tumour profile** includes pathological (i.e., grade) and molecular features of a tumour and gene expression patterns that reflect behaviour. These can be:
  - predictive factors
  - prognostic factors
  - companion diagnostic marker
- **Patient profile** includes terms related to the host of the cancer. These can be demographic factors, such as age and gender, or acquired, such as immunodeficiency and performance status.
- **Environment/social determinates of health** may include treatment-related and patient education, expertise, access, ageism and healthcare delivery) and quality of management. The WHO has listed examples as follows: income and social protection, education, unemployment and job insecurity, working life conditions, food insecurity, housing, basic amenities and the environment, early childhood development, social inclusion and non-discrimination, structural conflict and access to affordable health services of decent quality.[23]

When describing prognostic factors, it is important to state what outcome the factors are prognostic for and at what point in the patient trajectory. The anatomical extent of disease as described by TNM stage defines prognosis for survival.

In the second edition of the *UICC TNM Classification of Malignant Tumours* for each tumour site, grids were developed that identified prognostic factors for survival at the time of diagnosis and whether they were considered to be essential, additional, or new and promising.[17] The grids were updated for the third edition[18] and have been further updated and incorporated into the ninth edition of the *UICC Manual of Clinical Oncology*.[24] Essential factors are those that are required in addition to the anatomical extent of disease to determine treatment as identified by published clinical practice guidelines. The table is a generic example of the prognostic factors' summary grid and has been revised and updated.

Within the 'tumour-related' column of the grid, no attempt has been made to distinguish between predictive factors, prognostic factors and companion diagnostic markers. It should be noted with the rapid changes in medical knowledge that, in particular the relevant important molecular features that influence prognosis may not be the most current.

Given that environment and social determinants of health are consistent across all tumour sites, this column has been simplified so not all factors are included. Given the rapid changes in knowledge, the new and promising row can quickly become outdated as newer factors are identified and previously promising factors

may be shown not to be relevant; therefore, this row has been eliminated. The grids included are not exhaustive and are not available for some less common tumours.

Prognostic factors	Tumour related	Host related	Environment related
Essential*	TNM Histological type R Status	Age Comorbidities Sex	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Tumour bulk Tumour marker level Molecular and genetic markers	Race, gender Smoking history, Alcohol consumption Obesity Level of education	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery
New and promising	Molecular markers Gene expression patterns	Germline *mutation*	

* The origin of essential factors as imperatives for treatment decisions are from known and available clinical practice guidelines.

Essential TNM

Information on the anatomical extent of disease or stage at presentation is central to cancer surveillance to establish cancer burden as it provides additional valuable information to incidence, survival and mortality data.[25] However, cancer registries particularly in low- and middle-income countries frequently have insufficient information to determine complete TNM data, either because of inability to perform necessary investigations or because of lack of recording of information [26]. In view of this, the UICC TNM Project has with the International Agency for Research in Cancer developed 'Essential TNM' that can be used to collect stage data by cancer registrars, when complete TNM information is not available. Essential TNM flowcharts were originally developed for breast, cervix, colon, and prostate carcinomas and have been expanded to now include also oesophageal, hepatocellular, ovarian carcinomas and lymphomas. The User's Guide to Essential TNM is available for download at https://publications.iarc.fr/ and www.uicc.org.

Paediatric Tumours

Since the fourth edition, the UICC TNM Classification of Malignant Tumours has not incorporated any classifications of paediatric tumours. This decision has stemmed from the lack of an international standard staging system for many paediatric tumours. To enable stage data collection by population-based cancer registries, there needs to be agreement on cancer staging. Recognition of this led to a consensus meeting held in 2014 and resulted in the publication of recommendations on the staging of paediatric malignancies for the purposes of population surveillance.[27] The classifications published are not intended to replace the classifications used by the clinician when treating an individual patient but instead to facilitate the collection of stage by population-based cancer registries.

Related Classifications

Since 1958, WHO has been involved in a programme aimed at providing internationally acceptable criteria for the histological diagnosis of tumours. This has resulted in the *International Histological Classification of Tumours,* which contains, in an illustrated multivolume series, definitions of tumour types and a proposed nomenclature. A new series, *WHO Classification of Tumours – Pathology and Genetics of Tumours,* continues this effort. (Information on these publications is at www.iarc.fr.)

The *WHO International Classification of Diseases for Oncology (ICD-O-4)*[21] is a coding system for neoplasms by topography and morphology and for indicating behaviour (e.g., malignant, benign). In the interest of promoting national and international collaboration in cancer research and specifically of facilitating cooperation in clinical investigations, it is recommended that the WHO *Classification of Tumours* be used for classification and definition of tumour types and that the ICD-O-4 code be used for storage and retrieval of data.

Definitions of Additional Terms Used in Cancer Staging[28]

1. Cancer stage (a noun) – 'the stage'
   The UICC has defined the term 'stage' as the anatomical extent of disease.
2. Cancer staging (a verb) – 'to stage'
   It refers to the process of deriving the 'stage'. This includes the investigational work-up, most usually examination and imaging studies, or alternatively, verifying or consulting the T-, N- and M- category definitions and combinations.
3. Stage migration
   The term 'stage migration' describes a change in the proportion of T, N, or M categories following the introduction of new means of assessing disease extent in populations of patients rather than in individual patients. Please see prostate (page 188) for further discussion and example of capturing method of detection.
4. Stage shift
   The term 'stage shift' describes a change in the pattern of stage distribution within a defined population to a lower stage following the introduction of early detection or screening programs or to a higher stage when access to care becomes limited.

5. Downstaging/downsizing/upstaging/understaging
   - The term 'downstaging' is used to describe a reduction in T or N category after neoadjuvant therapy
   - The term 'downsizing' is used to describe a reduction in the size of tumour after neoadjuvant therapy
   - The terms 'upstaging' and 'understaging' are occasionally used and typically relate to different diagnostic accuracies of various staging investigations. We do not recommend their use.

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Substantial changes in the 2025 ninth edition compared to the 2017 eighth edition are marked by a bar at the left-hand side of the page.

A TNM web page with Frequently Asked Questions (FAQs) and a form for submitting questions or comments on the TNM can be found at https://www.uicc.org.
Readers are encouraged to visit https://www.uicc.org for updates and errata.

Head and Neck Tumours

Introductory Notes

The following sites are included:

- Oral cavity (including mucosal lip)*
- Pharynx: oropharynx (HPV associated and HPV independent), nasopharynx, hypopharynx
- Larynx: supraglottis, glottis, subglottis
- Nasal cavity and paranasal sinuses (maxillary and ethmoid sinus, but not sphenoid or frontal sinuses)
- Unknown primary carcinoma – cervical lymph nodes
- Malignant melanoma of upper aerodigestive tract
- Salivary glands (major and minor)
- Thyroid gland
- Parathyroid

Note

* The dry lip and vermillion border of the lip (C00.0, C00.1, C00.2) and commissure (C00.6) are included in skin of the head and neck (page 138).

Carcinomas arising in minor salivary glands of the upper aerodigestive tract are classified according to the rules for tumours of salivary glands. One tumour involving two anatomical sites is classified according to the site in which the greater part of the tumour is located unless specific sites of origin are identifiable from histology. HPV-associated carcinomas overlapping oral cavity and oropharynx are generally classified as arising from the oropharynx.

Each site is described under the following headings:

- Anatomical sites and subsites where appropriate
- Definition of the regional lymph nodes
- Clinical TNM (cTNM) classification
- Pathological TNM (pTNM) classification
- Stage
- Prognostic factors grid.

Regional Lymph Nodes

Midline nodes are considered ipsilateral nodes except in the thyroid.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Oral Cavity and Mucosal Lip
(ICD-O-4, C00.3-5, C02-06)

The definitions of the T,N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to carcinomas (excluding carcinomas of minor salivary glands) of the mucosal surfaces of the lips and of the oral cavity. For vermillion border of the lip, see page 138)

There should be histological confirmation of the disease.

Anatomical Sites and Subsites

Oral Cavity including Mucosal Lip (ICD-O-4 C00.3-5, C02.0-C02.3, C02.9, C03-C06)*

1. Buccal mucosa
   a) Mucosa of upper and lower lips (C00.3-5)*
   b) Cheek mucosa (C06.0)
   c) Retromolar areas (C06.2)
   d) Buccoalveolar sulci, upper and lower (vestibule of mouth) (C06.1)
2. Upper alveolus and gingiva (upper gum) (C03.0)
3. Lower alveolus and gingiva (lower gum) (C03.1)
4. Hard palate (C05.0)
5. Tongue**
   a) Dorsal surface and lateral borders anterior to circumvallate papillae (anterior two-thirds) (C02.0, 1)
   b) Inferior (ventral) surface (C02.2)
6. Floor of mouth (C04)

Notes

* The dry lip and vermillion border of the lip (C00.0, C00.1, C00.2) and commissure (C00.6) are included in skin of the head and neck (page 138).

****** Base of tongue/lingual tonsil C02.4), posterior to circumvallate papillae, is classified in the oropharynx.

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

Clinical TNM Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour 2 cm or less in greatest dimension and 5 mm or less depth of invasion [1,2]

cT2 Tumour 2 cm or less in greatest dimension and more than 5 mm depth of invasion or
Tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion not more than 10 mm

cT3 Tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion more than 10 mm
or
Tumour more than 4 cm in greatest dimension and not more than 10 mm depth of invasion

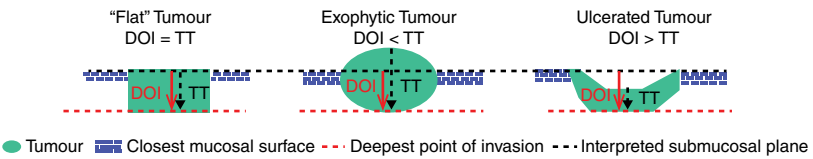
cT4a Tumour more than 4 cm in greatest dimension and more than 10 mm depth of invasion
or
Tumour invades through the cortical bone (with involvement of spongiosa/spongy bone) of the mandible or maxilla or involves the maxillary sinus, or invades the skin of the face [2]

cT4b Tumour invades masticator space, pterygoid plates or skull base, or encases internal carotid artery

Notes

[1] Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumour as cT4a.

[2] Superficial invasion of adjacent skin (i.e., dry vermillion and vermillion border of the lip) from mucosal lip is not sufficient to be classified as a T4a tumour.



- Black dotted line: IMP ("Interpreted Mucosal Plane"): a plane just beneath the closest intact surface of normal mucosa
- Red solid arrow: DOI ("Depth of Invastion"): measured from IMP to deepest point of invasion
- Black dotted arrow: TT (Tumour thickness): measured from centre of tumour surface to the deepest point of invasion

Schematic figure depicting the difference between radiological depth of invasion (DOI) and tumour thickness (TT) for clinical T category determination. Reproduced with thanks to Shao Hui Huang.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without clinical extranodal extension
cN2 Metastasis described as:
- cN2a Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without clinical extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, not more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2c Metastasis in bilateral or contralateral lymph nodes, not more than 6 cm in greatest dimension, without clinical extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without clinical extranodal extension
cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Pathological TNM Classification

The pT categories correspond to the clinical cT categories. For pM, see page 8.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without pathological extranodal extension
pN2 Metastasis described as:

pN2a Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension with pathological extranodal extension*

or

Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension without pathological extranodal extension

pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without pathological extranodal extension

pN3b Metastasis in a single lymph node more than 3 cm in greatest dimension with pathological extranodal extension*

or

Metastasis in multiple ipsilateral, or any contralateral or bilateral node(s) with pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T4a	N0, N1	M0
	T1, T2, T3, T4a	N2	M0
Stage IVB	Any T	N3	M0
	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid – Oral Cavity

Prognostic factors for carcinoma of the oral cavity

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Surgical resection margin Lymphovascular invasion	Performance status Smoking during radiotherapy	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Tumour budding, tumour hypoxia, lymph node ratio, extensive perineural invasion Worst pattern of invasion PD-L1 status Tumour grade Perineural invasion	Age, co-morbidity, Betel or areca nut chewing	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Pharynx
(ICD-O-4 C01, C02.4, C05.1-2, C09, C10.0, C10.2-3, C10.9, C11-13)

Rules for Classification

The classification applies only to carcinomas (excluding carcinomas of minor salivary glands). There should be histological confirmation of the disease.

Anatomical Sites and Subsites

Nasopharynx (C11)

1. Posterosuperior wall: extends from the level of the junction of the hard and soft palates to the base of the skull (C11.0, 1)
2. Lateral wall: including the fossa of Rosenmüller (C11.2)
3. Inferior wall: consists of the superior surface of the soft palate (C11.3).

Note
The margin of the choanal orifices, including the posterior margin of the nasal septum, is included with the nasal fossa.

Oropharynx (ICD-O-4 C01, C02.4, C05.1-2, C09.0-1, 9, C10.0, C10.2-3, C10.9)

1. Anterior wall (glossoepiglottic area)
   a) Base of tongue (posterior to the vallate papillae or posterior third) (C01)
   b) Vallecula (C10.0)
   c) Lingual Tonsil (C02.4)
2. Lateral wall (C10.2)
   a) Tonsil (C09.9)
   b) Tonsillar fossa (C09.0) and tonsillar (faucial) pillars (C09.1)
   c) Glossotonsillar sulci (tonsillar pillars) (C09.1)
3. Posterior wall (C10.3)
4. Superior wall
   a) Inferior surface of soft palate (C05.1)
   b) Uvula (C05.2)

Hypopharynx (C12, C13)

1. Piriform sinus (C12.9): extends from the pharyngoepiglottic fold to the upper end of the oesophagus. It is bounded laterally by the thyroid cartilage and medially by the hypopharyngeal surface of the aryepiglottic fold (C13.1) and the arytenoid and cricoid cartilages.
2. Pharyngo-oesophageal junction (postcricoid area) (C13.0): extends from the level of the arytenoid cartilages and connecting folds to the inferior border of the cricoid cartilage, thus forming the anterior wall of the hypopharynx.

3. Posterior pharyngeal wall (C13.2): extends from the superior level of the hyoid bone (or floor of the vallecula) to the level of the inferior border of the cricoid cartilage and from the apex of one piriform sinus to the other.

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

Clinical TNM Classification

Nasopharynx (C11)

The definitions of the T,N and M categories correspond with the AJCC version.

T – Primary Tumour

cTX Primary tumour cannot be assessed

cT0 No evidence of primary tumour, but EBV-positive (EBV-associated) cervical node(s) metastasis present

cTis Carcinoma in situ

cT1 Tumour confined to nasopharynx
or
Tumour extends to oropharynx and/or nasal cavity without parapharyngeal involvement

cT2 Tumour with extension to parapharyngeal space
or
Tumour infiltration of the medial pterygoid, lateral pterygoid and/or prevertebral muscles

cT3 Tumour invades bony structures of skull base, cervical vertebrae, pterygoid structures and/or paranasal sinuses

cT4 Tumour with any of the following:
- Intracranial extension
- Unequivocal clinical and/or radiological involvement of cranial nerves
- Involvement of hypopharynx
- Invading orbit (including inferior orbital fissure)
- Involvement of parotid gland
- Infiltration beyond the anterolateral surface of the lateral pterygoid muscle

N – Regional Nodes

cNX Regional lymph nodes cannot be assessed

cN0 No regional lymph node metastasis

cN1 Unilateral metastasis in cervical lymph node(s), and/or unilateral or bilateral metastasis in retropharyngeal lymph nodes, and 6 cm or less in greatest dimension, and above the caudal border of cricoid cartilage, and without advanced clinical/radiological extranodal extension*

cN2 Bilateral metastasis in cervical lymph nodes, and 6 cm or less in greatest dimension, and above the caudal border of cricoid cartilage, and without advanced clinical/radiological extranodal extension*

cN3 Metastasis in cervical lymph node(s) greater than 6 cm in greatest dimension
or
Extension below the caudal border of cricoid cartilage
or
Advanced clinical/radiological extranodal extension*

Notes

* Advanced radiological and/or clinical extranodal extension is unequivocal evidence of tumour invasion into adjacent structures (i.e., skin, muscle, salivary gland and/or neurovascular bundles) identified by appropriate morphological imaging or clinical examination.
Midline nodes are considered ipsilateral nodes.

The pT, pN, and pM1 categories correspond to the cT, cN, and cM1 categories. Extranodal extension however is defined pathologically not clinically or radiologically. As treatment for the primary is invariably non-surgical pT category is rarely appropriate.

M – Distant Metastasis

cM0 No distant metastasis
M1 Distant metastasis.
M1a Distant metastasis. Three or fewer lesion(s) in one or more organs
M1b Distant metastasis of more than three lesions in one or more organs

Stage – Nasopharynx

Stage 0	Tis	N0	M0
Stage IA	T1, T2	N0	M0
Stage IB	T0, T1, T2	N1	M0
Stage II	T0, T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage III	T4	Any N	M0
	Any T	N3	M0
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Reference

1 Pan JJ, Mai HQ, Ng WT, et al. Ninth version of the AJCC and UICC nasopharyngeal cancer TNM staging classification. *JAMA Oncol.* (2024); 10(12): 1627–1635. doi: https://doi.org/10.1001/jamaoncol.2024.4354.

Oropharynx – HPV Associated

The definitions of the T, N and M categories are new and are expected to correspond with the AJCC 9th version.

T – Primary Tumour

cT0 No evidence of primary tumour, but p16 positive (HPV-associated) cervical node(s) metastasis present

cT1 Tumour 2 cm or less in greatest dimension*
cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension
cT3 Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
cT4 Tumour invades any of the following: larynx**, deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), medial or lateral pterygoid muscle, hard palate, mandible, pterygoid plates (medial and/or lateral), nasopharynx, skull base, encases carotid artery

Notes

* The anatomical structure of the tonsillar crypts and lingual tonsil means that the basement membrane is incomplete and no carcinoma in situ is recognised.

** Mucosal extension to lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in ipsilateral lymph node(s), all 6 cm or less in greatest dimension, without unequivocal imaging-detected and/or clinical extranodal extension
cN2 Metastasis in ipsilateral lymph node(s), all 6 cm or less in greatest dimension, with unequivocal imaging-detected and/or clinical extranodal extension*
or
Contralateral or bilateral metastasis in lymph node(s), all 6 cm or less in greatest dimension without unequivocal imaging-detected and/or clinical extranodal extension
cN3 Metastasis in lymph node(s) greater than 6 cm in greatest dimension
or
Contralateral or bilateral metastasis in lymph node(s) with unequivocal imaging-detected and/or clinical extranodal extension*

Notes

* Imaging-detected extranodal extension (iENE) on appropriate morphological imaging refers to unequivocal radiologic signs of tumour invasion through the capsule of a lymph node into either perinodal fat or adjacent tissues (e.g. skin, muscle or neurovascular structures) or a coalescent nodal mass, which comprises ≥2 adjacent lymph nodes with loss of their intervening tissue planes and capsules to merge into a single indivisible structure.

Clinical extranodal extension is defined as per ***Oral Cavity and Mucosal Lip*** on page 20.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

Pathological TNM Classification

The pT categories correspond to the cT categories. For pM, see page 8.

pN – Regional Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in 1–4 lymph nodes without definitive pathologic extranodal extension
- pN1a Metastasis in 1 lymph node without definitive pathological extranodal extension
- pN1b Metastasis in 2–4 lymph nodes without definitive pathological extranodal extension

pN2
1–4 lymph nodes with definitive pathologic extranodal extension
or
Metastasis in >4 lymph nodes without definitive pathological extranodal extension

pN3 Metastasis in >4 lymph nodes with definitive pathological extranodal extension

Notes

Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage Oropharynx – HPV Associated

Clinical

Stage I	T0, T1, T2	N0, N1	M0
Stage II	T0, T1, T2	N2	M0
	T3	N0, N1, N2	M0
Stage III	Any T	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Pathological

Stage I	T0, T1, T2	N0, N1a, N1b	M0
Stage II	T0, T1, T2	N2, N3	M0
	T3	N0, N1a, N1b, N2	M0
Stage III	T3	N3	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Reference

1 Huang SH, Su J, Koyfman SA, et al. A proposal for HPV-associated oropharyngeal carcinoma in the ninth edition clinical TNM classification. *JAMA Otolaryngol Head Neck Surg.* (2025); 151(7): 1–10. doi: https://doi.org/10.1001/jamaoto.2025.0848.

Oropharynx – HPV Independent

The definitions of the T,N and M categories correspond with the AJCC 8th edition/ version.

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour 2 cm or less in greatest dimension
cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension
cT3 Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
cT4a Tumour invades any of the following: larynx,* deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), medial pterygoid, hard palate, mandible
cT4b Tumour invades any of the following: lateral pterygoid muscle, pterygoid plates, nasopharynx, skull base; or encases carotid artery

Note

* Mucosal extension to the lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of the larynx.

Hypopharynx

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour limited to one subsite of hypopharynx (see pages 24 and 25) and 2 cm or less in greatest dimension

cT2 Tumour invades more than one subsite of hypopharynx or an adjacent site
or
Tumour measures more than 2 cm but not more than 4 cm in greatest dimension, *without* fixation of hemilarynx

cT3 Tumour more than 4 cm in greatest dimension
or
Tumour *with* fixation of hemilarynx
or
Tumour with extension to oesophageal mucosa

cT4a Tumour invades any of the following: thyroid/cricoid cartilage, hyoid bone, thyroid gland, oesophagus beyond the mucosa, central compartment soft tissue*

cT4b Tumour invades prevertebral fascia, encases carotid artery or invades mediastinal structures

Notes

* Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.
Midline nodes are considered ipsilateral nodes.

Oropharynx – HPV Independent and Hypopharynx

N – Regional Nodes

cNX Regional lymph nodes cannot be assessed

cN0 No regional lymph node metastasis

cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without clinical extranodal extension

cN2 Metastasis described as:

- cN2a Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without clinical extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without clinical extranodal extension

cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

Pathological TNM Classification

The pT categories correspond to the cT categories. For pM, see page 8.

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

Oropharynx – HPV Independent and Hypopharynx

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without pathological extranodal extension
pN2 Metastasis described as:
- pN2a Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension with pathological extranodal extension*
  or
  Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without pathological extranodal extension
- pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension
- pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
pN3b Metastasis in a single lymph node more than 3 cm in greatest dimension with pathological extranodal extension*
or
Metastasis in multiple ipsilateral or any contralateral or bilateral node(s) with pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage HPV-Independent Oropharynx and Hypopharynx

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T1, T2, T3	N2	M0
	T4a	N0, N1, N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid

Nasopharynx

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Histological type	Age Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Plasma EBV-DNA copy number Gross tumour volume Site of metastases SUV_{max} PD-L1 status	Co-morbidities	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Oropharynx

HPV-associated oropharyngeal carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Surgical resection margin	Performance status Smoking during radiotherapy	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	HPV genotype Tumour volume Hypoxia PD-L1 status	Age, co-morbidities	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

HPV-independent oropharyngeal carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Surgical resection margin	Smoking during radiotherapy	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Number of involved nodes Tumour volume Hypoxia PD-L1 status	Age, co-morbidities	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Hypopharynx

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Surgical resection margin	Smoking during radiotherapy	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Number of involved nodes Tumour volume Hypoxia PD-L1 status	Age, co-morbidities	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

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1 Pan JJ, Ng WT, Zong J F, et al. Proposal for the 8th edition of the AJCC/UICC staging system for nasopharyngeal cancer in the era of intensity-modulated radiotherapy. *Cancer* 2016; 122: 546–558.

2 O'Sullivan B, Huang SH, Su J, et al. A proposal for UICC/AJCC pre-treatment TNM staging for HPV-related oropharyngeal cancer by the International Collaboration on Oropharyngeal Cancer Network for Staging (*ICON-S*): A comparative multi-centre cohort study. *Lancet Oncol* 2016; 17: 440–451.

Larynx
(ICD-O-4 C32.0-2, C10.1)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas (excluding carcinomas of minor salivary glands). There should be histological confirmation of the disease.

Anatomical Sites and Subsites

1. Supraglottis (C32.1)
   a) Suprahyoid epiglottis [including tip, lingual (anterior) (C10.1) and laryngeal surfaces]
   b) Aryepiglottic fold, laryngeal aspect
   c) Arytenoid
   d) Infrahyoid epiglottis
   e) Ventricular bands (false cords)

   Epilarynx (including marginal zone)

   Supraglottis excluding epilarynx
2. Glottis (C32.0)
   a) Vocal cords
   b) Anterior commissure
   c) Posterior commissure
3. Subglottis (C32.2)

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

Clinical TNM Classification

T – Primary Tumour

Supraglottis

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ

cT1 Tumour limited to one subsite of supraglottis with normal vocal cord mobility

cT2 Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of piriform sinus) without fixation of the larynx

cT3 Tumour limited to larynx with vocal cord fixation and/or invades any of the following: post-cricoid area, pre-epiglottic space, paraglottic space and/or inner cortex of thyroid cartilage

cT4a Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid or oesophagus

cT4b Tumour invades prevertebral space, encases carotid artery or invades mediastinal structures

Glottis

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
- T1a Tumour limited to one vocal cord
- T1b Tumour involves both vocal cords

cT2 Tumour extends to supraglottis and/or subglottis and/or with impaired vocal cord mobility

cT3 Tumour limited to larynx with vocal cord fixation and/or invades paraglottic space and/or inner cortex of the thyroid cartilage

cT4a Tumour invades through the outer cortex of the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus

cT4b Tumour invades prevertebral space, encases carotid artery or mediastinal structures

Subglottis

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour limited to subglottis

cT2 Tumour extends to vocal cord(s) with normal or impaired mobility

cT3 Tumour limited to larynx with vocal cord fixation

cT4a Tumour invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus and styloglossus), strap muscles, thyroid, oesophagus

cT4b Tumour invades prevertebral space, encases carotid artery or invades mediastinal structures

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without clinical extranodal extension
cN2 Metastasis described as:
- cN2a Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without clinical extranodal extension
cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

Pathological TNM Classification

The pT categories correspond to the clinical cT categories. For pM, see page 8.

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

pN – Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without pathological extranodal extension
pN2 Metastasis described as:

pN2a Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension, with pathological extranodal extension*
or
Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without pathological extranodal extension

pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

pN3b Metastasis in a single lymph node more than 3 cm in greatest dimension with pathological extranodal extension*
or
Metastasis in multiple ipsilateral or any contralateral or bilateral node(s) with pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T4a	N0, N1	M0
	T1, T2, T3, T4a	N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid

Prognostic factors for survival for laryngeal and hypopharyngeal carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Vocal cord mobility Surgical resection margin	Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Number of cartilage involvement Regions/subsites involved Tumour volume PD-L1 status	Co-morbidities Age Gender Baseline laryngeal function	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Nasal Cavity and Paranasal Sinuses
(ICD-O-4 C30.0, C31.0-1)

The definitions of the T,N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to carcinomas (excluding carcinomas of minor salivary glands). There should be histological confirmation of the disease.

Anatomical Sites and Subsites

1. Nasal cavity (C30.0)
   - Septum
   - Floor
   - Lateral wall
   - Vestibule
2. Maxillary sinus (C31.0)
3. Ethmoid sinus (C31.1)
   - Left
   - Right

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

Clinical TNM Classification

T – Primary Tumour

Maxillary Sinus

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour limited to the mucosa with no erosion or destruction of bone
cT2 Tumour causing bone erosion or destruction, including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
cT3 Tumour invades any of the following: bone of posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa or ethmoid sinuses

cT4a Tumour invades any of the following: anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate and sphenoid or frontal sinuses

cT4b Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx or clivus

Nasal Cavity and Ethmoid Sinus

cTX Primary tumour cannot be assessed
CT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour restricted to one subsite of nasal cavity or ethmoid sinus, with or without bony invasion

cT2 Tumour involves two subsites in a single site or extends to involve an adjacent site within the nasoethmoidal complex, with or without bony invasion

cT3 Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate or cribriform plate

cT4a Tumour invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses

cT4b Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx or clivus

N – Regional Lymph Nodes

cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without clinical extranodal extension

cN2 Metastasis described as:

- cN2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension or

cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Pathological TNM Classification

The pT categories correspond to the clinical T categories. For pM, see page 8.

The pN categories correspond to the cN categories. Extranodal extension however is defined pathologically not clinically or radiologically.

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

pN – Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without pathological extranodal extension
pN2 Metastasis described as:
- pN2a Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension with pathological extranodal extension*
  or
  Metastasis in a single lymph node more than 3 cm but not more than 6 cm in greatest dimension, without pathological extranodal extension
- pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension
- pN2c Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without pathological extranodal extension
pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with pathological extranodal extension*
or
Metastasis in multiple ipsilateral or any contralateral or bilateral node(s) with pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T1, T2, T3	N2	M0
	T4a	N0, N1, N2	M0
Stage IVB	T4b	Any N	M0
	Any T	N3	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid – Nasal Cavity and Paranasal Sinuses

Prognostic factors for paranasal sinus tumours

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Surgical resection margin	Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Histotype PD-L1 status HPV/p16 status	Age	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Unknown Primary – Cervical Nodes

Rules for Classification

There should be histological confirmation of squamous cell carcinoma with lymph node metastases but without an identified primary carcinoma. Histological methods should be used to identify EBV and HPV/p16-associated tumours. If there is evidence of EBV, the nasopharyngeal classification is applied. If there is evidence of HPV and/or positive immunohistochemistry p16 overexpression, the p16-positive oropharyngeal classification is applied.

Clinical TNM Classification

EBV Negative and HPV Independent or Unknown

The definitions of the N and M categories correspond with the AJCC 8th edition/version.

T – Primary Tumour

T0 No evidence of primary tumour

N – Regional Lymph Nodes

cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without clinical extranodal extension

cN2 Metastasis described as:

- cN2a Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension
- cN2c Metastasis in bilateral lymph nodes, none more than 6 cm in greatest dimension, without clinical extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without clinical extranodal extension

cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Notes

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging is becoming a standard method of detecting unequivocal extranodal extension.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Pathological TNM Classification

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes. For pM, see page 8.

pN1 Metastasis in a single lymph node, 3 cm or less in greatest dimension without pathological extranodal extension
pN2 Metastasis described as:
- pN2a Metastasis in a single lymph node, 3 cm or less in greatest dimension with pathological extranodal extension* or more than 3 cm but not more than 6 cm in greatest dimension without pathological extranodal extension
- pN2b Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension
- pN2c Metastasis in bilateral lymph nodes, none more than 6 cm in greatest dimension, without pathological extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without pathological extranodal extension
pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with pathological extranodal extension* or multiple ipsilateral, or any contralateral, or bilateral node(s) with pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage

Stage III	T0	N1	M0
Stage IVA	T0	N2	M0
Stage IVB	T0	N3	M0
Stage IVC	T0	N1, N2, N3	M1

Clinical TNM Classification

HPV Associated

The definitions of the N and M categories are expected to correspond with the AJCC 9th version.

T – Primary Tumour

T0 No evidence of primary tumour

N – Regional Lymph Nodes

See HPV-Associated Oropharynx cN (page 27)

Pathological TNM Classification

T0 No evidence of primary tumour.

pN – Regional Lymph Nodes

See HPV-Associated Oropharynx pN (page 28)

Stage

Clinical

Stage I	T0	N1	M0
Stage II	T0	N2	M0
Stage III	T0	N3	M0
Stage IV	T0	N1, N2, N3	M1

Pathological

Stage I	T0	N1	M0
Stage II	T0	N2, N3	M0
Stage IV	T0	N1, N2	M1

Clinical TNM Classification

EBV Positive

The definitions of the N and M categories are expected to correspond with the AJCC 9th version.

T – Primary Tumour

T0 No evidence of primary tumour

N – Regional Lymph Nodes

See Nasopharynx cN classification (pages 25 and 26)

Note

Midline nodes are considered ipsilateral nodes.

Pathological TNM Classification

Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

The pN categories correspond to the nasopharynx cN categories, except that extranodal extension is defined pathologically, and evidence of structural (skin, muscle, salivary gland and/or neurovascular bundles) involvement is required.

M – Distant Metastasis

cM0 No distant metastasis
M1 Distant metastases
M1a: 1–3 metastatic lesions
M1b: >3 metastatic lesions

Stage

Stage I	T0	N1	M0
Stage II	T0	N2	M0
Stage III	T0	N3	M0
Stage IV	T0	N1, N2, N3	M1

Prognostic Factors Grid – Cervical Nodes Unknown Primary

Prognostic factors for head and neck unknown primary.

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Histology N category M category p16/HPV status, or EBV DNA status	Immunosuppression (especially skin cancer)	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Tumour differentiation or grade Location of nodal disease (above vs below clavicle) PD-L1 status	Gender Haemoglobin level Smoking history	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Malignant Melanoma of Upper Aerodigestive Tract (ICD-O-4 C00-06, C09-14, C30-32)

The definitions of the T, N and M categories correspond to the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to mucosal malignant melanomas of the head and neck region, i.e., of the upper aerodigestive tract. There should be histological confirmation of the disease and division of cases by site.

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour.

Clinical TNM Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT3 Tumour limited to the epithelium and/or submucosa (mucosal disease)
cT4a Tumour invades deep soft tissue, cartilage, bone or overlying skin
cT4b Tumour invades any of the following: brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space and mediastinal structures

Note
Mucosal melanomas are aggressive tumours; therefore, T1 and T2 are omitted as are stages I and II.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Pathological TNM Classification

The pT and pN categories correspond to the cT and cN categories. For pM, see page 8.

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

Stage

Stage III	T3	N0	M0
Stage IVA	T4a	N0	M0
	T3, T4a	N1	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid – Malignant Melanoma of Upper Aerodigestive Tract

Prognostic factors for Malignant Melanoma of Upper Aerodigestive Tract.

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Depth of invasion Surgical resection margin	Co-morbidity Age	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Site of primary Tumour Size Tumour mitotic rate Ulceration BRAF mutation status		Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factor.

Source: Shuman AG, Light E, Olsen SH, et al. Mucosal melanoma of the head and neck: predictors of prognosis. *Archives of Otolaryngology – Head & Neck Surgery* 2011; 137(4): 331–337.

Heppt MV, Roesch A, Weide B, et al. Prognostic factors and treatment outcomes in 444 patients with mucosal melanoma. *European Journal of Cancer* 2017; 81: 36-44.

Moya-Plana A, Auperin A, Obongo R, et al. Oncologic outcomes, prognostic factor analysis and therapeutic algorithm evaluation of head and neck mucosal melanomas in France. *European Journal of Cancer* 2019; 123: 1–10.

Salivary Glands
(ICD-O-4 C00-C14, C15.0, C15.3, C30-C33, C41.1)

The definitions of the T, N and M categories are new and are expected to correspond with the AJCC 9th version.

Rules for Classification

The classification applies only to carcinomas of the salivary glands. There should be histological confirmation of the disease.

Anatomical Sites Include

- Parotid gland (C07.9)
- Submandibular (submaxillary) gland (C08.0)
- Sublingual gland (C08.1)
- Minor salivary glands (C00-C06, C09-14, C15.0, C15.3, C30-33, C41.1)

Regional Lymph Nodes

The regional lymph nodes are the cervical nodes.

Clinical TNM Classification

T – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cT1	Tumour 2 cm or less in greatest dimension without extraparenchymal extension*
cT2	Tumour more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension*
cT3	Tumour more than 4 cm, or gross extraparenchymal or adjacent site mucosal/soft tissue extension beyond site without structural involvement
cT4a	Tumour invades immediately adjacent structures, including skin, bone**, cartilage, solid organ parenchyma, oesophagus, trachea, and/or named nerve
cT4b	Tumour invades beyond adjacent structures, e.g. encasement of carotid artery, and/or base of skull invasion (except nasopharynx), and/or spinal column invasion, and/or intracranial invasion, and/or orbital apex, and/or prevertebral space, and/or mediastinal structures, and/or masticator space, etc.

Notes

* Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues or nerve, except those listed under T4a and T4b. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes.

** Destruction of intrinsic sinus bones is not considered bone invasion for skull base tumors. Erosion of cortical bone is not considered bone invasion; a minor salivary gland tumor arising within the bone is not considered bone invasion.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–3 ipsilateral lymph node(s) without unequivocal imaging-detected or clinical extranodal extension
cN2 Metastasis in more than 3 lymph nodes or any lymph node with unequivocal imaging-detected and/or clinical extranodal extension*

Notes

* Extranodal extension can be detected clinically or radiologically. Imaging-detected extranodal extension (iENE) on appropriate morphological imaging refers to unequivocal radiologic signs of tumour invasion through the capsule of a lymph node into either perinodal fat or adjacent tissues (e.g. skin, muscle or neurovascular structures) or a coalescent nodal mass (A coalescent nodal mass comprises ≥2 adjacent lymph nodes that have lost their intervening tissue planes and capsules to merge into a single indivisible structure).

Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Imaging-detected unequivocal extranodal extension is becoming standard.

Midline nodes are considered ipsilateral nodes.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the clinical cT categories. For pM, see page 8.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen should ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes. Negative pathological examination of fewer lymph nodes is acceptable for pN0 designation.

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in 1–3 lymph node without definitive pathological extranodal extension
pN2 Metastasis in >3 lymph nodes
or
Metastasis in any lymph node with definitive pathological extranodal extension*

Notes

* Pathological extranodal extension (pENE) should only be diagnosed when tumour that is present within the confines of a lymph node definitively transgresses through the entire thickness of the lymph node capsule into the surrounding connective tissue, with or without stromal reaction.

A soft tissue deposit should be considered as at least one lymph node with extranodal extension if it occurs at a site where a regional lymph node would be expected.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3, T4	N0	M0
	T1, T2	N1	M0
Stage IIIB	T1, T2	N2	M0
	T3, T4	N1, N2	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid – Salivary Glands

Prognostic factors for salivary gland tumour survival

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Histologic aggression type and grade Tumour size Local invasion Perineural invasion Surgical resection margin	Age	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Nodal metastases Molecular markers	Facial palsy, pain	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Thyroid Gland
(ICD-O-4 C73.9)

The definitions of the T, N and M categories correspond to the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas. There should be microscopic confirmation of the disease and division of cases by histological type.

Regional Lymph Nodes

The regional lymph nodes are the cervical and upper/superior mediastinal nodes.

Clinical TNM Classification

T – Primary Tumour*

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour 2 cm or less in greatest dimension, limited to the thyroid
- cT1a Tumour 1 cm or less in greatest dimension, limited to the thyroid
- cT1b Tumour more than 1 cm but not more than 2 cm in greatest dimension, limited to the thyroid

cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension, limited to the thyroid

cT3 Tumour more than 4 cm in greatest dimension, limited to the thyroid or with gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid or omohyoid muscles) or parathyroid gland
- cT3a Tumour more than 4 cm in greatest dimension, limited to the thyroid
- cT3b Tumour of any size with gross extrathyroidal extension invading strap muscles (sternohyoid, sternothyroid, thyrohyoid or omohyoid muscles) or parathyroid gland

cT4a Tumour extends beyond the thyroid capsule and invades any of the following: subcutaneous soft tissues, larynx, trachea, oesophagus, recurrent laryngeal nerve or the sternocleidomastoid muscle.

cT4b Tumour invades the prevertebral fascia, mediastinal vessels or encases the carotid artery.

Note

* Including papillary, follicular, poorly differentiated, Hürthle cell and anaplastic carcinomas.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis
- cN1a Metastasis in Level VI (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes) or upper/superior mediastinum
- cN1b Metastasis in other unilateral, bilateral or contralateral cervical (Levels I, II III, IV or V) or retropharyngeal

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Pathological TNM Classification

The pT and pN categories correspond to the cT and cN categories. For pM, see page 8.

pN0 Histological examination of a selective neck dissection specimen should ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Histopathological Types

The four major histopathological types are:
- Papillary carcinoma (including those with follicular foci)
- Follicular carcinoma (including so-called Hürthle cell carcinoma)
- Medullary carcinoma
- Anaplastic

Stage

Separate stage groupings are recommended for papillary and follicular (including differentiated, oncocytic (Hürthle) cell and poorly differentiated), medullary and anaplastic (undifferentiated) carcinomas:

Papillary and Follicular (Younger than 55 Years)

Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1

Papillary or Follicular (55 Years and Older)

Stage I	T1a,T1b,T2	N0	M0
Stage II	T3	N0	M0
	T1,T2,T3	N1	M0
Stage III	T4a	Any N	M0
Stage IVA	T4b	Any N	M0
Stage IVB	Any T	Any N	M1

Medullary

Stage I	T1a, T1b	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T1, T2, T3	N1a	M0
Stage IVA	T1, T2, T3	N1b	M0
	T4a	Any N	M0
Stage IVB	T4b	Any N	M0
Stage IVC	Any T	Any N	M1

Anaplastic

Stage IVA	T1,T2,T3a	N0	M0
Stage IVB	T1,T2,T3a	N1	M0
Stage IVB	T3b,T4a,T4b	N0,N1	M0
Stage IVC	Any T	Any N	M1

Prognostic Factors Grid – Papillary and Follicular Thyroid Carcinoma

Prognostic factors for survival in differentiated thyroid carcinoma of follicular cell derivation

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Size and number of nodal metastases Site, size and number distant metastases Post-treatment thyroglobulin Radioactive iodine uptake Histological Subtype	Age	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status

(Continued)

(Continued)

Prognostic factors	Tumour related	Host related	Environment related*
Additional	Angioinvasion *BRAF* ^{V600E} mutation** Molecular profile	Gender	Expertise of a treatment at the specific level (e.g., surgery and nuclear medicine) Access to information R status after surgery

* Essential for Anaplastic Thyroid Carcinoma.

** See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Prognostic Factors Grid – Medullary Carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Pre- and postoperative calcitonin and CEA Familial vs Sporadic MEN germline mutation	Age	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Calcitonin doubling time Ki-67 proliferative index Tumour necrosis Molecular profile		Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Parathyroid Gland
(ICD-O-4 C75.0)

The definitions of the T, N and M categories correspond to the AJCC 8th edition/version.

Rules for Classification

This classification applies only to carcinomas of the parathyroid gland.

Regional Lymph Nodes

The regional lymph nodes are the cervical and upper/superior mediastinal nodes

Clinical TNM Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
cT1 Limited to the parathyroid gland or any tumour with minimal extra-parathyroid soft tissue extension without direct invasion of the thyroid gland
cT2 Tumour of any size with invasion into the thyroid gland
cT3 Tumour of any size with invasion into adjacent skeletal muscle, recurrent laryngeal nerve, trachea, oesophagus, thymus or direct invasion into adjacent lymph node(s)
cT4 Tumour of any size with direct invasion into major blood vessels or spine

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1a Metastasis in Level VI (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes) or upper/superior mediastinal lymph nodes
cN1b Metastasis in other unilateral, bilateral or contralateral cervical (Levels I, II, III, IV or V) or retropharyngeal node

M – Distant Metastasis

cM0 No distance metastasis
cM1 Distance metastasis

Pathological TNM Classification

The pT and pN categories correspond to the cT and cN categories. For pM, see page 8.

Stage

There is no data to determine stage group definitions for carcinomas of the parathyroid gland.

Digestive System Tumours

Introductory Notes

The following sites and types are included:

- Oesophagus and oesophagogastric junction
- Stomach
- Small intestine
- Appendix
- Colon and rectum
- Anal canal and perianal skin
- Liver cell carcinoma
- Intrahepatic cholangiocarcinoma
- Gallbladder
- Perihilar bile duct
- Distal extrahepatic bile duct
- Ampulla of Vater
- Pancreas
- Neuroendocrine tumours

Regional Lymph Nodes

The number of lymph nodes ordinarily included in a lymphadenectomy specimen is noted at each site.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Oesophagus
(ICD-O-4 C15 including oesophagogastric junction C16.7)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas and includes adenocarcinomas of the oesophagogastric/gastroesophageal junction (excluding carcinomas of minor salivary glands of the upper third of the oesophagus). There should be histological confirmation of the disease and division of cases by topographic localisation and histological type. A tumour the epicentre of which is within 2 cm of the oesophagogastric junction and also extends into the oesophagus is classified and staged using the oesophageal scheme. Cancers involving the oesophagogastric junction (OGJ) whose epicentre is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers.

Anatomical Subsites

1. Cervical oesophagus (C15.0): This commences at the lower border of the cricoid cartilage and ends at the thoracic inlet (suprasternal notch), approximately 18 cm from the upper incisor teeth.
2. Intrathoracic oesophagus:
   a) The upper thoracic portion (C15.3) extending from the thoracic inlet to the level of the tracheal bifurcation, approximately 24 cm from the upper incisor teeth.
   b) The mid-thoracic portion (C15.4) is the proximal half of the oesophagus between the tracheal bifurcation and the oesophagogastric junction. The lower level is approximately 32 cm from the upper incisor teeth.
   c) The lower thoracic portion (C15.5), approximately 8 cm in length (includes abdominal oesophagus), is the distal half of the oesophagus between the tracheal bifurcation and the oesophagogastric junction. The lower level is approximately 40 cm from the upper incisor teeth.
3. Oesophagogastric junction (C16.7): Cancers involving the oesophagogastric junction (OGJ) whose epicentre is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers. Cancers whose epicentre is more than 2 cm distal from the OGJ will be staged using the stomach cancer TNM and stage even if the OGJ is involved.

Regional Lymph Nodes

The regional lymph nodes, irrespective of the site of the primary tumour, are those in the oesophageal drainage area including coeliac axis nodes and para-oesophageal nodes in the neck but not the supraclavicular nodes. These include cervical peri-oesophageal nodes, the lower cervical paratracheal nodes, the thoracic paratracheal nodes, the subcarinal nodes, the thoracic para-oesophageal nodes, pulmonary ligament nodes, the diaphragmatic nodes, adjacent to or behind the crura, the pericardial nodes, adjacent to the gastroesophageal junction, the left gastric nodes, the common hepatic nodes, the splenic nodes and the coeliac nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ/high-grade dysplasia

cT1 Tumour invades lamina propria, muscularis mucosae, or submucosa
- T1a Tumour invades lamina propria or muscularis mucosae
- T1b Tumour invades submucosa

cT2 Tumour invades muscularis propria
cT3 Tumour invades adventitia including peri-oesophageal fat
cT4 Tumour invades adjacent structures
- cT4a Tumour invades pleura, pericardium, azygos vein, diaphragm or peritoneum
- cT4b Tumour invades other adjacent structures such as aorta, vertebral body or trachea

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–2 regional lymph nodes
cN2 Metastasis in 3–6 regional lymph nodes
cN3 Metastasis in 7 or more regional lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include seven or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage and Prognostic Group – Carcinomas of the Oesophagus and Oesophagogastric Junction*

Squamous Cell Carcinoma

Clinical Stage*

Stage 0	Tis	N0	cM0
Stage I	T1	N0, N1	cM0
Stage II	T2	N0, N1	cM0
	T3	N0	cM0
Stage III	T1, T2	N2	cM0
	T3	N1, N2	cM0
Stage IVA	T4a, T4b	N0, N1, N2	cM0
	Any T	N3	cM0
Stage IVB	Any T	Any N	cM1

Pathological Stage*

Stage 0	pTis	pN0	cM0
Stage IA	pT1a	pN0	cM0
Stage IB	pT1b	pN0	cM0
Stage IIA	pT2	pN0	cM0
Stage IIB	pT1	pN1	cM0
	pT3	pN0	cM0
Stage IIIA	pT1	pN2	cM0
	pT2	pN1	cM0
Stage IIIB	pT2	pN2	cM0
	pT3	pN1, pN2	cM0
	pT4a	pN0, pN1	cM0
Stage IVA	pT4a	pN2	cM0
	pT4b	Any pN	cM0
	Any pT	pN3	cM0
Stage IVB	Any T	Any N	pM1

Pathological Prognostic Group

Group	T	N	M	Grade	Location
Group 0	pTis	pN0	cM0	N/A	Any
Group IA	pT1a	pN0	cM0	1, X	Any
Group IB	pT1a	pN0	cM0	2–3	Any
	pT1b	pN0	cM0	Any	Any
	pT2	pN0	cM0	1	Any
Group IIA	pT2	pN0	cM0	2–3, X	Any
	pT3	pN0	cM0	Any	Lower,
	pT3	pN0	cM0	1	Upper, middle
Group IIB	pT3	pN0	cM0	2–3	Upper, middle
	pT3	pN0	cM0	Any	X
	pT3	pN0	cM0	X	Any
	pT1	pN1	cM0	Any	Any
Group IIIA	pT1	pN2	cM0	Any	Any
	pT2	pN1	cM0	Any	Any
Group IIIB	pT2	pN2	cM0	Any	Any
	pT3	pN1, pN2	cM0	Any	Any
	pT4a	pN0, pN1	cM0	Any	Any
Group IVA	pT4a	pN2	cM0	Any	Any
	pT4b	Any pN	cM0	Any	Any
	Any pT	pN3	cM0	Any	Any
Group IVB	Any T	Any N	pM1	Any	Any

Adenocarcinoma
Clinical Stage*

	T	N	M
Stage 0	Tis	N0	cM0
Stage I	T1	N0	cM0
Stage IIA	T1	N1	cM0
Stage IIB	T2	N0	cM0
Stage III	T2	N1	cM0
	T3, T4a	N0, N1	cM0
Stage IVA	T1–T4a	N2	cM0
	T4b	N0, N1, N2	cM0
	Any T	N3	cM0
Stage IVB	Any T	Any N	cM1

Pathological Stage*

Stage 0	pTis	pN0	cM0
Stage IA	pT1a	pN0	cM0
Stage IB	pT1b	pN0	cM0
Stage IIA	pT2	pN0	cM0
Stage IIB	pT1	pN1	cM0
	pT3	pN0	cM0
Stage IIIA	pT1	pN2	cM0
	pT2p	pN1	cM0
Stage IIIB	pT2	pN2	cM0
	pT3	pN1, pN2	cM0
	pT4a	pN0, pN1	cM0
Stage IVA	pT4a	pN2	cM0
	pT4b	Any pN	cM0
	Any pT	pN3	cM0
Stage IVB	Any pT	Any pN	pM1

Note

* If the T or N category is clinical and the other category is pathological, the clinical stage should be used, unless the M category is pM1, in which case the pathological stage is used regardless of whether the T and N categories are pathological or clinical: e.g., for squamous cell carcinoma, pT2cN1 Stage as Clinical Stage II.

Pathological Prognostic Group

	T	N	M	Grade
Group 0	pTis	pN0	cM0	N/A
Group IA	pT1a	pN0	cM0	1, X
Group IB	pT1a	pN0	cM0	2
	pT1b	pN0	cM0	1, 2, X
Group IC	pT1a, pT1b	pN0	cM0	3
	pT2	pN0	cM0	1, 2
Group IIA	pT2	pN0	cM0	3, X
Group IIB	pT1	pN1	cM0	Any
	pT3	pN0	cM0	Any
Group IIIA	pT1	pN2	cM0	Any
	pT2	pN1	cM0	Any
Group IIIB	pT2	pN2	cM0	Any
	pT3	pN1,pN2	cM0	Any
	pT4a	pN0,pN1	cM0	Any

(Continued)

	T	N	M	Grade
Group IVA	pT4a pT4b Any pT	pN2 Any pN pN3	cM0 cM0 cM0	Any Any Any
Group IVB	Any T	Any N	pM1	Any

Notes

The AJCC publishes prognostic groups for adenocarcinoma and squamous cell carcinoma after neoadjuvant therapy (categories with the prefix 'y').

A modified Ryan classification of pathological assessment after neoadjuvant therapy may be used.[1]

Prognostic Factors Grid – Oesophagus

Prognostic factors for survival in oesophageal cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Presence of lympho-vascular invasion (LVI), extranodal extension Resection margin Mismatch repair (MMR) status (adenocarcinoma)	Performance status Age Nutritional status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education
Additional	Adenocarcinoma: HER2, MMR, PD-L1 status Squamous cell: PD-L1 status		Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Takeda FR, Tustumi F, de Almeida Obregon C, et al. Prognostic value of tumor regression grade based on Ryan score in squamous cell carcinoma and adenocarcinoma of esophagus. *Ann Surg Oncol* 2020; 27(4): 1241–1247. doi:https://doi.org/10.1245/s10434-019-07967-8.

Stomach
(ICD-O-4 C16 excluding C16.7)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease. Cancers involving the oesophagogastric junction (OGJ) whose epicentre is within the proximal 2 cm of the cardia (Siewert types I/II) are to be staged as oesophageal cancers. Cancers whose epicentre is more than 2 cm distal from the OGJ will be staged using the stomach cancer TNM and stage even if the OGJ is involved.

The changes in this edition from the seventh edition are based on recommendations from the International Gastric Cancer Association Staging Project.[1]

Anatomical Subsites

1. Cardia (C16.0)
2. Fundus (C16.1)
3. Corpus (C16.2)
4. Antrum (C16.3) and pylorus (C16.4)

Regional Lymph Nodes

The regional lymph nodes of the stomach are the perigastric nodes along the lesser and greater curvatures, the nodes along the left gastric, common hepatic, splenic and coeliac arteries, and the hepatoduodenal nodes.

Involvement of other intra-abdominal lymph nodes such as retropancreatic, mesenteric and para-aortic is classified as distant metastasis.

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ: intraepithelial tumour without invasion of the lamina propria, high-grade dysplasia
cT1	Tumour invades lamina propria, muscularis mucosae or submucosa
cT1a	Tumour invades lamina propria or muscularis mucosae
cT1b	Tumour invades submucosa
cT2	Tumour invades muscularis propria
cT3	Tumour invades subserosa

cT4 Tumour perforates serosa (visceral peritoneum) or invades adjacent structures[a,b,c]
- cT4a Tumour perforates serosa
- cT4b Tumour invades adjacent structures[a,b]

Notes

[a] The adjacent structures of the stomach are the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine and retroperitoneum.

[b] Intramural extension to the duodenum or oesophagus is classified by the depth of greatest invasion in any of these sites including stomach.

[c] Tumour that extends into gastrocolic or gastrohepatic ligaments or into greater or lesser omentum, without perforation of visceral peritoneum, is T3.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–2 regional lymph nodes
cN2 Metastasis in 3–6 regional lymph nodes
cN3 Metastasis in 7 or more regional lymph nodes
- cN3a Metastasis in 7–15 regional lymph nodes
- cN3b Metastasis in 16 or more regional lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

Note

Distant metastasis includes peritoneal seeding, positive peritoneal cytology, and omental tumour not part of continuous extension.

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 16 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Clinical Stage*

Stage 0	Tis	N0	cM0
Stage I	T1, T2	N0	cM0
Stage IIA	T1, T2	N1, N2, N3	cM0
Stage IIB	T3, T4a	N0	cM0
Stage III	T3, T4a	N1,N2, N3	cM0
Stage IVA	T4b	Any N	cM0
Stage IVB	Any T	Any N	cM1

Pathological Stage*

Stage 0	pTis	pN0	cM0
Stage IA	pT1	pN0	cM0
Stage IB	pT1	pN1	cM0
	pT2	pN0	cM0
Stage IIA	pT1	pN2	cM0
	pT2	pN1	cM0
	pT3	pN0	cM0
Stage IIB	pT1	pN3a	cM0
	pT2	pN2	cM0
	pT3	pN1	cM0
	pT4a	pN0	cM0
Stage IIIA	pT2	pN3a	cM0
	pT3	pN2	cM0
	pT4a	pN1, pN2	cM0
	pT4b	pN0	cM0
Stage IIIB	pT1, pT2	pN3b	cM0
	pT3, pT4a	pN3a	cM0
	pT4b	pN1, pN2	cM0
Stage IIIC	pT3, pT4a	pN3b	cM0
	pT4b	pN3a, pN3b	cM0
Stage IV	Any T	Any N	pM1

Notes

* The AJCC publishes prognostic groups for use after neoadjuvant therapy (categories with the prefix 'y').

If the T or N category is clinical and the other category is pathological, the clinical stage should be used: e.g., pT2cN1 Stage as Clinical stage IIA.

Prognostic Factors Grid – Stomach

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Mismatch repair (MMR) status	Age, race Extent of resection	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education

(Continued)

Prognostic factors	Tumour related	Host related	Environment related*
Additional	Tumour site: cardia or distal stomach, histological type Lymphovascular invasion HER2, PD-L1 status, Claudin 18.2		Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.
Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Sano T, Coit D, Kim HH, et al. for the IGCA Staging Project. Proposal of a new stage grouping of gastric cancer for TNM classification: International Gastric Cancer Association Staging Project. *Gastric Cancer* 2017; 20: 217–225.

Small Intestine
(ICD-O-4 C17)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

Anatomical Subsites

1. Duodenum (C17.0)
2. Jejunum (C17.1)
3. Ileum (C17.2) (excludes ileocecal valve C18.0)

Note
This classification does not apply to carcinomas of the ampulla of Vater (see page 93).

Regional Lymph Nodes

The regional lymph nodes for the duodenum are the pancreaticoduodenal, pyloric, hepatic (pericholedochal, cystic, hilar) and superior mesenteric nodes.

The regional lymph nodes for the ileum and jejunum are the mesenteric nodes, including the superior mesenteric nodes and, for the terminal ileum only, the ileocolic nodes including the posterior caecal nodes.

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ

cT1	Tumour invades lamina propria, muscularis mucosae or submucosa
	cT1a Tumour invades lamina propria or muscularis mucosae
	cT1b Tumour invades submucosa
cT2	Tumour invades muscularis propria
cT3	Tumour invades subserosa or non-peritonealised perimuscular tissue (mesentery or retroperitoneum*) without perforation of the serosa
cT4	Tumour perforates visceral peritoneum or directly invades other organs or structures (includes other loops of small intestine, mesentery or retroperitoneum and abdominal wall by way of serosa; for duodenum only, invasion of pancreas)

Note

* The non-peritonealised perimuscular tissue is, for jejunum and ileum, part of the mesentery and, for duodenum in areas where serosa is lacking, part of the retroperitoneum.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–2 regional lymph nodes
cN2 Metastasis in 3 or more regional lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

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

Stage

Stage 0	Tis	N0	M0
Stage I	T1, T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4	N0	M0
Stage IIIA	Any T	N1	M0
Stage IIIB	Any T	N2	M0
Stage IV	Any T	Any N	M1

Appendix
(ICD-O-4 C18.1)

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies to adenocarcinomas and neuroendocrine carcinomas of the appendix. Well-differentiated neuroendocrine tumours are classified separately. There should be histological confirmation of the disease and separation of carcinomas into mucinous and non-mucinous adenocarcinomas.

Appendiceal goblet cell adenocarcinomas are classified according to the adenocarcinoma scheme.

Grading is of particular importance for mucinous tumours.

The following are the procedures for assessing T, N and M categories.

Anatomical Site

Appendix (C18.1)

Regional Lymph Nodes

The ileocolic are the regional lymph nodes.

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ: intraepithelial or invasion of lamina propria
cTis (LAMN)[a]	Low-grade appendiceal mucinous neoplasm confined to the muscularis propria; acellular mucin or mucinous epithelium may invade into the muscularis propria.
cT1	Tumour invades submucosa[b]
cT2	Tumour invades muscularis propria[b]
cT3	Tumour invades subserosa or mesoappendix
cT4	Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix, and/or directly invades other organs or structures[c]
cT4a	Tumour perforates visceral peritoneum, including mucinous peritoneal tumour or acellular mucin on the serosa of the appendix or mesoappendix
cT4b	Tumour directly invades other organs or structures

Notes

[a] The Tis(LAMN) category does not apply to HAMNs; HAMN are staged using the appendiceal adenocarcinoma T categories.

[b] T1 and T2 are not applicable to LAMN; acellular mucin or mucinous epithelium that extends into the subserosa or serosa should be classified as T3 or T4a, respectively.

[c] Direct invasion in T4 includes invasion of other intestinal segments by way of the serosa, e.g., invasion of ileum. Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1, 2 or 3.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–3 regional lymph nodes
- cN1a Metastasis in 1 regional lymph node
- cN1b Metastases in 2–3 regional lymph nodes
- cN1c Tumour deposit(s), i.e., satellites,* in the subserosa, or in non-peritonealised pericolic or peri-rectal soft tissue *without* regional lymph node metastasis

cN2 Metastasis in 4 or more regional lymph nodes

Notes

* Tumour deposits (TDs) represent discrete tumour nodules of any shape, contour or size in peri-rectal and peri-colonic fat, away from the leading edge of the tumour, within the lymph drainage area of the primary carcinoma. TDs can originate from different histological structures, including lymph nodes, vessels and nerves. Therefore, TDs may contain foci of extramural vascular invasion (EMVI) and perineural invasion (PNI). The feature distinguishing a TD from EMVI and PNI is the presence of unequivocal tumour extension from the vessel or nerve into the surrounding fat or fibroconnective tissue.

When tumour outgrowth from EMVI and/or PNI is present, the diagnosis of TDs and EMVI/PNI should be denoted separately in the report. If the tumour involves an identifiable lymph node, it is considered as lymph node metastasis and not as TDs even if the tumour extends into the perinodal fat.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Intraperitoneal acellular mucin only
- cM1b Intraperitoneal metastasis only, including mucinous epithelium
- cM1c Non-peritoneal metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0	
Stage 0	Tis (LAMN)	N0	M0	
Stage I	T1, T2	N0	M0	
Stage IIA	T3	N0	M0	
IIB	T4a	N0	M0	
IIC	T4b	N0	M0	
Stage IIIA	T1, T2	N1	M0	
IIIB	T3, T4	N1	M0	
IIIC	Any T	N2	M0	
Stage IVA	Any T	Any N	M1a	Any G
	Any T	Any N	M1b	G1
IVB	Any T	Any N	M1b	G2, G3, GX
Stage IVC	Any T	Any N	M1c	Any G

Colon and Rectum
(ICD-O-4 C18-20 excluding C18.1)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing the T, N and M categories.

Anatomical Sites and Subsites

Colon (C18)

1. Caecum (C18.0)
2. Ascending colon (C18.2)
3. Hepatic flexure (C18.3)
4. Transverse colon (C18.4)
5. Splenic flexure (C18.5)
6. Descending colon (C18.6)
7. Sigmoid colon (C18.7)

Rectosigmoid junction (C19)
Rectum (C20)

Regional Lymph Nodes

For each anatomical site or subsite, the following are regional lymph nodes:

Caecum	ileocolic, right colic
Ascending colon	ileocolic, right colic, middle colic
Hepatic flexure	right colic, middle colic
Transverse colon	right colic, middle colic, left colic, inferior mesenteric
Splenic flexure	middle colic, left colic, inferior mesenteric
Descending colon	left colic, inferior mesenteric
Sigmoid colon	sigmoid, left colic, superior rectal (haemorrhoidal), inferior mesenteric and rectosigmoid
Rectum	superior, middle, and inferior rectal (haemorrhoidal), inferior mesenteric, internal iliac, mesorectal (paraproctal), lateral sacral, presacral and sacral promontory (Gerota)

Metastasis in nodes other than those listed here is classified as distant metastasis.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ: invasion of lamina propria[a]

cT1 Tumour invades submucosa
cT2 Tumour invades muscularis propria
cT3 Tumour invades subserosa or into non-peritonealised pericolic or peri-rectal tissues
cT4 Tumour directly invades other organs or structures[b,c,d] and/or perforates visceral peritoneum
- cT4a Tumour perforates visceral peritoneum
- cT4b Tumour directly invades other organs or structures

Notes

[a] Tis includes cancer cells confined within the mucosal lamina propria (intramucosal) with no extension through the muscularis mucosae into the submucosa.

[b] Invades through to visceral peritoneum to involve the surface.

[c] Direct invasion in T4b includes invasion of other organs or segments of the colorectum by way of the serosa, as confirmed on microscopic examination, or for tumours in a retroperitoneal or subperitoneal location, direct invasion of other organs or structures by virtue of extension beyond the muscularis propria.

[d] Tumour that is adherent to other organs or structures, macroscopically, is classified cT4b. However, if no tumour is present in the adhesion, microscopically, the classification should be pT1-3, depending on the anatomical depth of wall invasion.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–3 regional lymph nodes
- cN1a Metastasis in 1 regional lymph node
- cN1b Metastasis in 2–3 regional lymph nodes
- cN1c Tumour deposit(s), i.e. satellites,* in the subserosa, or in non-peritonealised pericolic or peri-rectal soft tissue *without* regional lymph node metastasis

cN2 Metastasis in 4 or more regional lymph nodes
- cN2a Metastasis in 4–6 regional lymph nodes
- cN2b Metastasis in 7 or more regional lymph nodes

Notes

* TDs represent discrete tumour nodules of any shape, contour or size in peri-rectal and peri-colonic fat, away from the leading edge of the tumour, within the lymph drainage area of the primary carcinoma. TDs can originate from different histological structures, including lymph nodes, vessels and nerves. Therefore, TDs may contain foci of extramural vascular invasion (EMVI) and perineural invasion (PNI). The feature distinguishing a TD from EMVI and PNI is the presence of unequivocal tumour extension from the vessel or nerve into the surrounding fat or fibroconnective tissue.

When tumour outgrowth from EMVI and/or PNI is present, the diagnosis of TDs and EMVI/PNI should be denoted separately in the report. If the tumour involves an identifiable lymph node, it is considered as lymph node metastasis and not as TDs even if the tumour extends into the perinodal fat.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Metastasis confined to one organ (liver, lung, ovary, non-regional lymph node(s)) without peritoneal metastases
- cM1b Metastasis in more than one organ
- cM1c Metastasis to the peritoneum with or without other organ involvement

TNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0
Stage I	T1, T2	N0	M0
Stage II	T3, T4	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T4a	N0	M0
Stage IIC	T4b	N0	M0
Stage III	Any T	N1, N2	M0
Stage IIIA	T1, T2	N1	M0
	T1	N2a	M0
Stage IIIB	T1, T2	N2b	M0
	T2, T3	N2a	M0
	T3, T4a	N1	M0
Stage IIIC	T3, T4a	N2b	M0
	T4a	N2a	M0
	T4b	N1, N2	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b
Stage IVC	Any T	Any N	M1c

Notes

* For patients treated with neoadjuvant therapy, the prefix 'y' is used to describe the yT, yN and y Stage. There is no separate stage classification.

A modified Ryan classification of pathological assessment after neoadjuvant therapy may be used.[1,2]

Prognostic Factors Grid – Colon and Rectum

Prognostic factors for survival in differentiated colorectal cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Circumferential margin (rectal cancer) Carcinoembryonic antigen (CEA) in blood, mismatch repair (MMR) status	Age Performance Status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education
Additional	Presence and location of Vascular/lymphatic invasion Perineural invasion Grade Tumour budding Perforation Tumour-stroma ratio (TSR) *KRAS*, *NRAS*, *BRAF*, *HER2*, NTRK RET fusion, POLE / POLD1 mutation	Race	Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

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1 Ryan R, Gibbons D, Hyland JM, et al. Pathological response following long-course neoadjuvant chemo-radiotherapy for locally advanced rectal cancer. Histopathology 2005; 47(2): 141–146.

2 College of American Pathologists. Protocol for the Examination of Specimens from Patients with Primary Carcinoma of the Colon and Rectum. Version: Colon Rectum 4.0.1.0. https://documents.cap.org/protocols/cp-gilower-colonrectum-17protocol-4010.pdf.

Anal Canal and Perianal Skin
(ICD-O-4 C21)

The anal canal extends from rectum to perianal skin (to the junction with hair-bearing skin). It is lined by the mucous membrane overlying the internal sphincter, including the transitional epithelium and dentate line. Tumours of anal margin and perianal skin defined as within 5 cm of the anal margin (ICD-O-4 C21.3) are classified with carcinomas of the anal canal.

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease and division of cases by histological type.

Regional Lymph Nodes

The regional lymph nodes are the peri-rectal, the internal iliac, external iliac and the inguinal lymph nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ, high-grade squamous intraepithelial lesion (HSIL), anal intraepithelial neoplasia II–III (AIN II–III) anal squamous intraepithelial neoplasia H (ASIN-H)[1]

cT1 Tumour 2 cm or less in greatest dimension
cT2 Tumour more than 2 cm but not more than 5 cm in greatest dimension
cT3 Tumour more than 5 cm in greatest dimension
cT4 Tumour of any size invades adjacent organ(s), e.g., vagina, urethra or bladder[2]

Notes

[1] AJCC does not include Tis.

[2] Direct invasion of the rectal wall, perianal skin, subcutaneous tissue or the sphincter muscle(s) *alone* is not classified as T4.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in regional lymph node(s)
- N1a Metastases in inguinal, mesorectal and/or internal iliac nodes
- N1b Metastases in external iliac nodes
- N1c Metastases in external iliac and in inguinal, mesorectal and/or internal iliac nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional peri-rectal/pelvic lymphadenectomy specimen should ordinarily include 12 or more lymph nodes; histological examination of an inguinal lymphadenectomy specimen should ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T1, T2	N1	M0
Stage IIIA	T3	N0, N1	M0
Stage IIIB	T4	N0	M0
Stage IIIC	T4	N1	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid – Anal Canal

Prognostic factors for outcome in anal cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	T, N and M categories	Age Male gender Immune suppression Performance status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education.
Additional	Skin ulceration, sphincter involvement Anal vs perianal	Long-term corticosteroids HIV status, viral load Herpes simplex virus status/p16 expression	Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang.

Liver
(ICD-O-4 C 22.0)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to hepatocellular carcinoma (HCC).

Cholangio- (intrahepatic bile duct) carcinoma and combined hepatocellular and cholangiocarcinoma (mixed hepatocellular/cholangiocellular carcinoma) of the liver have a separate classification (see page 85). There should be histological confirmation of the disease.

Hepatoblastoma classification is given in the paediatric chapter (see page 241).

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

The regional lymph nodes are the hilar, hepatic (along the proper hepatic artery), periportal (along the portal vein), inferior phrenic, and caval nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

- cT1a Solitary tumour 2 cm or less in greatest dimension with or without vascular invasion
- cT1b Solitary tumour more than 2 cm in greatest dimension without vascular invasion

cT2 Solitary tumour with vascular invasion more than 2 cm dimension or multiple tumours, none more than 5 cm in greatest dimension
cT3 Multiple tumours any more than 5 cm in greatest dimension
cT4 Tumour(s) involving a major branch of the portal or hepatic vein or with direct invasion of adjacent organs (including the diaphragm), other than the gallbladder or with perforation of visceral peritoneum

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include three or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Liver

Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
Stage IVA	Any T	N1	M0
Stage IVB	Any T	Any N	M1

Note

The Barcelona Clinic Liver Stage (BCLS), frequently used in the management of HCC, is a prognostic group system incorporating liver function and performance status. (BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update. Reig, Maria et al., *Journal of Hepatology*, Volume 76, Issue 3, 681–693.)

Prognostic Factors Grid – Liver (Hepatocellular Carcinoma)

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Major vascular invasion Microvascular invasion Size >5 cm multiple (vs single) Tumour differentiation AFP level	Age, performance status Fibrosis of underlying liver Tumour growth rate. Patient performance status. Liver function (Child–Pugh Class) Cirrhosis. Barcelona Clinic Liver Stage Degree of portal hypertension	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education. Resection Margin
Additional	NASH-HCC	Hepatitis activity	Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy, including transplantation and ablative procedures) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Intrahepatic Bile Ducts
(ICD-O-4 C22.1)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The staging system applies to intrahepatic cholangiocarcinoma and combined hepatocellular and cholangiocarcinoma (mixed hepatocellular/cholangiocellular carcinoma).

Regional Lymph Nodes

For right-liver intrahepatic cholangiocarcinoma, the regional lymph nodes include the hilar (common bile duct, hepatic artery, portal vein, and cystic duct), periduodenal, and peripancreatic lymph nodes.

For left-liver intrahepatic cholangiocarcinoma, regional lymph nodes include hilar and gastrohepatic lymph nodes.

For intrahepatic cholangiocarcinoma, spread to the coeliac and/or periaortic and caval lymph nodes is classified as distant metastases (M1).

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ (intraductal tumour)

cT1 Solitary tumour without vascular invasion
- cT1a Solitary tumour 5 cm or less in greatest dimension without vascular invasion
- cT1b Solitary tumour more than 5 cm in greatest dimension without vascular invasion

cT2 Solitary tumour with intrahepatic vascular invasion or multiple tumours, with or without vascular invasion
cT3 Tumour perforating the visceral peritoneum
cT4 Tumour involving local extrahepatic structures by direct hepatic invasion

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

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

Stage – Intrahepatic Bile Ducts

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

Gallbladder
(ICD-O-4 C23.9 and C24.4)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to carcinomas of gallbladder (C23.9) and cystic duct (C24.4). There should be histological confirmation of the disease.

Regional Lymph Nodes

Regional lymph nodes are the hepatic hilus nodes (including nodes along the common bile duct, hepatic artery, portal vein, and cystic duct).

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour invades lamina propria or muscular layer
- cT1a Tumour invades lamina propria
- cT1b Tumour invades muscular layer

cT2 Tumour invades perimuscular connective tissue; no extension beyond serosa or into liver
- cT2a Tumour invades perimuscular connective tissue on the peritoneal side with no extension to the serosa
- cT2b Tumour invades perimuscular connective tissue on the hepatic side with no extension into the liver

cT3 Tumour perforates the serosa (visceral peritoneum) and/or directly invades the liver and/or one other adjacent organ or structure, such as stomach, duodenum, colon, pancreas, omentum or extrahepatic bile ducts

cT4 Tumour invades main portal vein or hepatic artery or invades two or more extrahepatic organs or structures

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastases to 1–3 regional nodes
cN2 Metastasis to 4 or more regional nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

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

Stage – Gallbladder

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1, T2, T3	N1	M0
Stage IVA	T4	N0, N1	M0
Stage IVB	Any T	N2	M0
	Any T	Any N	M1

Perihilar Bile Ducts
(ICD-O-4 C24.3)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies to carcinomas of the extrahepatic bile ducts of perihilar localisation (Klatskin tumour). Included are the right, left and the common hepatic ducts.

Anatomical Sites and Subsites

Perihilar cholangiocarcinomas are tumours located in the extrahepatic biliary tree proximal to the origin of the cystic duct.

Regional Lymph Nodes

The regional nodes are the hilar and pericholedochal nodes in the hepatoduodenal ligament.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour confined to the bile duct, with extension up to the muscle layer or fibrous tissue
cT2a Tumour invades beyond the wall of the bile duct to surrounding adipose tissue
cT2b Tumour invades adjacent hepatic parenchyma
cT3 Tumour invades unilateral branches of the portal vein or hepatic artery
cT4 Tumour invades the main portal vein or its branches bilaterally, or the common hepatic artery, or unilateral second-order biliary radicals with contralateral portal vein or hepatic artery involvement

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastases to 1–3 regional lymph nodes
cN2 Metastases to 4 or more regional nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 15 more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Perihilar Bile Ducts

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2a, T2b	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
Stage IIIC	Any T	N1	M0
Stage IVA	Any T	N2	M0
Stage IVB	Any T	Any N	M1

Distal Extrahepatic Bile Duct
(ICD-O-4 C24.2)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies to carcinomas of the extrahepatic bile ducts distal to the insertion of the cystic duct. Cystic duct carcinoma is included under gallbladder.

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

The regional lymph nodes are along the common bile duct, hepatic artery, back toward the coeliac trunk, posterior and anterior pancreaticoduodenal nodes, and nodes along the superior mesenteric artery.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour invades bile duct wall to a depth less than 5 mm
cT2 Tumour invades bile duct wall to a depth of 5 mm up to 12 mm
cT3 Tumour invades bile duct wall to a depth of more than 12 mm
cT4 Tumour involves the coeliac axis, the superior mesenteric artery and/or the common hepatic artery

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastases
cN1 Metastases to 1–3 regional nodes
cN2 Metastasis to 4 or more regional nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the regional lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Distal Extrahepatic Bile Duct

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0, N1	M0
Stage IIIA	T1, T2, T3	N2	M0
Stage IIIB	T4	Any N	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid – Biliary Tract and Gallbladder Cancers

Prognostic risk factors in biliary tract carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Histology Grade, location Resection margin	Performance status Age	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education
Additional	Lymphovascular invasion Primary biliary cirrhosis BRAF, HER2, MMR, KRAS, RET, FGFR2, IDH Mutations		Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Ampulla of Vater
(ICD-O-4 C24.1)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

The regional lymph nodes are the same as for the head of the pancreas and are the lymph nodes along the common bile duct, common hepatic artery, portal vein, pyloric, infrapyloric, subpyloric, proximal mesenteric, coeliac, posterior and anterior pancreaticoduodenal vessels, and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery.

Note

The splenic lymph nodes and those of the tail of the pancreas are not regional; metastases to these lymph nodes are coded M1.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1a Tumour limited to ampulla of Vater or sphincter of Oddi
cT1b Tumour invades beyond the sphincter of Oddi (perisphincteric invasion) and/or into the duodenal submucosa
cT2 Tumour invades the muscularis propria of the duodenum
cT3 Tumour invades pancreas or peripancreatic tissue
- cT3a Tumour invades 5 mm or less into the pancreas
- cT3b Tumour invades more than 5 mm into the pancreas or extends into peripancreatic tissue or duodenal serosa but without involvement of the celiac axis or the superior mesenteric artery

cT4 Tumour with vascular involvement of the superior mesenteric artery or celiac axis, or common hepatic artery

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in 1–3 regional lymph nodes
cN2 Metastasis in 4 or more regional lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Ampulla of Vater

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b, T2	N0	M0
Stage IIA	T3a	N0	M0
Stage IIB	T3b	N0	M0
Stage IIIA	T1a, T1b, T2, T3	N1	M0
Stage IIIB	Any T	N2	M0
Stage IIIB	T4	Any N	M0
Stage IV	Any T	Any N	M1

Pancreas
(ICD-O-4 C25)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies to carcinomas of the exocrine pancreas and/or high-grade neuroendocrine carcinomas. Well-differentiated neuroendocrine tumours of the pancreas are classified as shown on page 104. There should be histological or cytological confirmation of the disease.

Anatomical Subsites

C25.0 Head of pancreas[a]
C25.1 Body of pancreas[b]
C25.2 Tail of pancreas[c]
C25.3 Pancreatic duct

Notes

[a] Tumours of the head of the pancreas are those arising to the right of the left border of the superior mesenteric vein. The uncinate process is considered as part of the head.

[b] Tumours of the body are those arising between the left border of the superior mesenteric vein and left border of the aorta.

[c] Tumours of the tail are those arising between the left border of the aorta and the hilum of the spleen.

Regional Lymph Nodes

The regional lymph nodes for tumours in the head and neck of the pancreas are the lymph nodes along the common bile duct, common hepatic artery, portal vein, pyloric, infrapyloric, subpyloric, proximal mesenteric, coeliac, posterior and anterior pancreaticoduodenal vessels, and along the superior mesenteric vein and right lateral wall of the superior mesenteric artery.

The regional lymph nodes for tumours in body and tail are the lymph nodes along the common hepatic artery, coeliac axis, splenic artery, and splenic hilum, as well as retroperitoneal nodes and lateral aortic nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ*

cT1 Tumour 2 cm or less in greatest dimension
- cT1a Tumour 0.5 cm or less in greatest dimension
- cT1b Tumour greater than 0.5 cm and not more than 1 cm in greatest dimension
- cT1c Tumour greater than 1 cm but not more than 2 cm in greatest dimension

cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension
cT3 Tumour more than 4 cm in greatest dimension
cT4 Tumour involves coeliac axis, superior mesenteric artery and/or common hepatic artery

Note
* Tis also includes the 'PanIN–III' classification.

cN – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastases in 1–3 regional lymph node(s)
cN2 Metastases in 4 or more regional lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage – Pancreas

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1, T2, T3	N1	M0
Stage III	T1, T2, T3	N2	M0
	T4	Any N	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid – Pancreas

Prognostic risk factors for pancreatic cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Extent of arterial (coeliac, common hepatic and gastric) involvement Resection margin CA19-9 level	Age Performance status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education
Additional	Number of metastases CA19-9 level NTRK gene fusion BRCA and PALB2 (germline and somatic) MMR, BRAF		Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Well-Differentiated Neuroendocrine Tumours of the Gastrointestinal Tract

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

This classification system applies to well-differentiated neuroendocrine tumours (carcinoid tumours and atypical carcinoid tumours) of the gastrointestinal tract, including the pancreas. Neuroendocrine tumours of the lung should be classified according to criteria for carcinoma of the lung. Merkel cell carcinoma of the skin has a separate classification.

Poorly differentiated neuroendocrine carcinomas (including small-cell neuroendocrine carcinoma and large-cell neuroendocrine carcinoma) are excluded and should be classified according to criteria for classifying carcinomas at the respective site.

Histopathological Grading

The following grading scheme has been proposed for all gastrointestinal well-differentiated neuroendocrine tumours:

Grade	Mitotic count (per 2 mm^2)[a]	Ki-67 index (%)[b]
G1	<2	<3
G2	2–20	3–20
G3	>20	>20

Notes

[a] per 2 mm^2 is equivalent to 10 HPF (high-power fields) – at least 40 fields (at 40× magnification) evaluated in areas of highest mitotic density.

[b] MIB1 antibody; % of 500–2000 tumour cells in areas of highest nuclear labelling.

The final grade is determined by whichever of the mitotic count or Ki-67 is higher.

Well-Differentiated Neuroendocrine Tumours – Stomach, Duodenum/Ampullary Tumours, Jejunum/Ileum, Appendix, Colon and Rectum

Regional Lymph Nodes

The regional lymph nodes correspond to those listed under the appropriate sites for carcinoma.

TNM Clinical Classification

Stomach (C16)

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour invades mucosa or submucosa and 1 cm or less in greatest dimension
cT2 Tumour invades muscularis propria or is more than 1 cm in greatest dimension
cT3 Tumour invades subserosa
cT4 Tumour perforates visceral peritoneum (serosa) or invades other organs or adjacent structures

Note
For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- M1a Hepatic metastasis(es) only
- M1b Extrahepatic metastasis(es) only
- M1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

TNM Clinical Classification

Duodenal/Ampullary Tumours (C17.0, C24.1)

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 *Duodenal:* Tumour invades mucosa or submucosa and 1 cm or less in greatest dimension
Ampullary: Tumour 1 cm or less in greatest dimension and confined within the sphincter of Oddi
cT2 *Duodenal:* Tumour invades muscularis propria or is more than 1 cm in greatest dimension
Ampullary: Tumour invades through sphincter into duodenal submucosa or muscularis propria, or more than 1 cm in greatest dimension
cT3 Tumour invades the pancreas or peripancreatic adipose tissue
cT4 Tumour perforates visceral peritoneum (serosa) or invades other organs

Note
For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Hepatic metastasis(es) only
- cM1b Extrahepatic metastasis(es) only
- cM1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

TNM Clinical Classification

Jejunum/Ileum (C17.1-2, C17.8-9)

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour invades mucosa or submucosa and 1 cm or less in greatest dimension
cT2 Tumour invades muscularis propria or is greater than 1 cm in greatest dimension
cT3 Tumour invades through the muscularis propria into subserosal tissue without penetration of overlying serosa
cT4 Tumour perforates visceral peritoneum (serosa) or invades other organs or adjacent structures

Note

For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Less than 12 regional lymph node metastasis without mesenteric mass(es) greater than 2 cm in size
cN2 12 or more regional nodes and/or mesenteric mass(es) greater than 2 cm in maximum dimension

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Hepatic metastasis(es) only
- cM1b Extrahepatic metastasis(es) only
- cM1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	Any N	M0
	Any T	N1, N2	M0
Stage IV	Any T	Any N	M1

TNM Clinical Classification

Appendix (C18.1)
T – Primary Tumour[a]

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour 2 cm or less in greatest dimension
cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension
cT3 Tumour more than 4 cm or with subserosal invasion or involvement of the mesoappendix
cT4 Tumour perforates peritoneum or invades other adjacent organs or structures, other than direct mural extension to adjacent subserosa, e.g., abdominal wall and skeletal muscles[b]

Notes

[a] Poorly differentiated neuroendocrine carcinomas, mixed adenoneuroendocrine carcinomas and goblet cell adenocarcinoma, are excluded and should be classified according to criteria for classifying carcinomas.

[b] Tumour that is adherent to other organs or structures, macroscopically, is classified as T4. However, if no tumour is present in the adhesion, microscopically, the tumour should be classified as pT1-3 as appropriate.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Hepatic metastasis(es) only
- cM1b Extrahepatic metastasis(es) only
- cM1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen should ordinarily include 12 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

TNM Clinical Classification

Colon and Rectum (C18-C20 excluding C18.1)

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour invades lamina propria or submucosa or is no greater than 2 cm in size
  cT1a Tumour less than 1 cm in size
  cT1b Tumour 1 or 2 cm in size
cT2 Tumour invades muscularis propria or is greater than 2 cm in size
cT3 Tumour invades subserosa, or non-peritonealised pericolic or peri-rectal tissues
cT4 Tumour perforates the visceral peritoneum or invades other organs

Note
For any T, add (m) for multiple tumours.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
  cM1a Hepatic metastasis(es) only
  cM1b Extrahepatic metastasis(es) only
  cM1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage IIA	T2	N0	M0
Stage IIB	T3	N0	M0
Stage IIIA	T4	N0	M0
Stage IIIB	Any T	N1	M0
Stage IV	Any T	Any N	M1

Well-Differentiated Neuroendocrine Tumours – Pancreas (C25)

Rules for Classification

This classification system applies to well-differentiated functioning and non-functioning neuroendocrine tumours of the pancreas.

Poorly differentiated neuroendocrine carcinomas are excluded and should be classified according to criteria for classifying carcinomas of the pancreas.

Regional Lymph Nodes

The regional lymph nodes correspond to those listed under the appropriate sites for carcinoma.

TNM Clinical Classification

Pancreas (C25)

T – Primary Tumour[a]

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cT1 Tumour limited to pancreas,[b] 2 cm or less in greatest dimension
cT2 Tumour limited to pancreas[b] more than 2 cm but less than 4 cm in greatest dimension
cT3 Tumour limited to pancreas,[b] more than 4 cm in greatest dimension or tumour invading duodenum or bile duct.
cT4 Tumour invades adjacent organs (stomach, spleen, colon, adrenal gland) or the wall of large vessels (coeliac axis or the superior mesenteric artery)

Notes

[a] For any T, add (m) for multiple tumours.

[b] Invasion of adjacent peripancreatic adipose tissue is accepted but invasion of adjacent organs is excluded.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- cM1a Hepatic metastasis(es) only
- cM1b Extrahepatic metastasis(es) only
- cM1c Hepatic and extrahepatic metastases

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2, T3	N0	M0
Stage III	T4	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

Lung, Pleural and Thymic Tumours

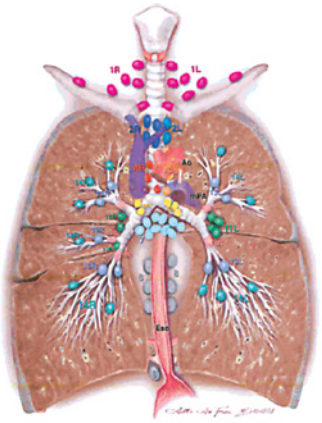
Introductory Notes

The classifications apply to carcinomas of the lung, including non-small-cell and small-cell carcinomas, bronchopulmonary carcinoid tumours, mesothelioma of the pleura and thymic tumours.

Regional Lymph Nodes

The regional lymph nodes extend from the supraclavicular region to the diaphragm (see Figure 1).[1] Direct extension of the primary tumour into lymph nodes is classified as lymph node metastasis.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.



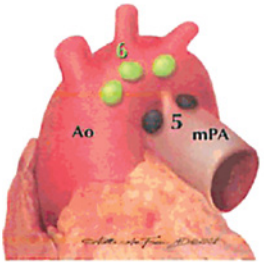
Supraclavicular zone
1 Low cervical, supraclavicular, and sternal notch nodes

SUPERIOR MEDIASTINAL NODES

Upper zone
2R Upper Paratracheal (right)
2L Upper Paratracheal (left)
3a Prevascular
3p Retrotracheal
4R Lower Paratracheal (right)
4L Lower Paratracheal (left)

AORTIC NODES

AP zone
5 Subaortic
6 Para-aortic (ascending aorta or phrenic)



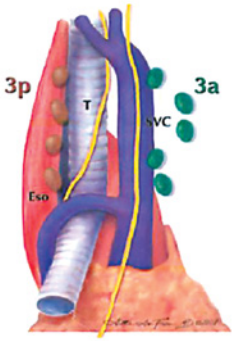
AORTIC NODES

AP zone
5 Subaortic
6 Para-aortic (ascending aorta or phrenic)

INFERIOR MEDIASTINAL NODES

Subcarinal zone
7 Subcarinal

Lower zone
8 Paraesophageal (below carina)
9 Pulmonary ligament



INFERIOR MEDIASTINAL NODES

Subcarinal zone
7 Subcarinal

Lower zone
8 Paraesophageal (below carina)
9 Pulmonary ligament

N1 NODES

Hilar/Interlobar zone
10 Hilar
11 Interlobar

Peripheral zone
12 Lobar
13 Segmental
14 Subsegmental

Figure 1 The International Association for the Study of Lung Cancer (IASLC) lymph node map. Source: Rusch et al.[1]/with permission of Elsevier.

Lung
(ICD-O-4 C34)

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies to carcinomas of the lung, including non-small-cell carcinomas, small-cell carcinomas and bronchopulmonary carcinoid tumours. It does not apply to sarcomas and other rare tumours.

Changes in this edition from the eighth edition are based on recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project (see references).[2–6]

There should be histological confirmation of the disease and division of cases by histological type.

Anatomical Subsites

1. Main bronchus (C34.0)
2. Upper lobe (C34.1)
3. Middle lobe (C34.2)
4. Lower lobe (C34.3)

Regional Lymph Nodes

The regional lymph nodes are the intrathoracic nodes (mediastinal, hilar, lobar, interlobar, segmental and subsegmental), scalene and supraclavicular lymph nodes.

TNM Clinical Classification

T – Primary Tumour*

cTX	Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualised by imaging or bronchoscopy
cT0	No evidence of primary tumour
cTis	Carcinoma in situ[a]
cT1	Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, or tumour in a lobar or more peripheral bronchus[b]
cT1mi	Minimally invasive adenocarcinoma[c]
cT1a	Tumour 1 cm or less in greatest dimension[b]
cT1b	Tumour more than 1 cm but not more than 2 cm in greatest dimension[b]
cT1c	Tumour more than 2 cm but not more than 3 cm in greatest dimension[b]

cT2a Tumour more than 3 cm but not more than 4 cm in greatest dimension **or**
Tumour not more than 4 cm in greatest dimension that invades one or more of the following:
- The main bronchus (up to the carina, but without involvement of the carina)
- Invades the visceral pleura
- An adjacent lobe
- Is associated with atelectasis or obstructive pneumonitis that extends to
- The hilar region either involving part of or the entire lung
- Invades an adjacent lobe

cT2b Tumour more than 4 cm but not more than 5 cm in greatest dimension

cT3 Tumour more than 5 cm but not more than 7 cm in greatest dimension or
Tumour not more than 7 cm that directly invades any of the following:
- Parietal pleura, chest wall (including superior sulcus tumours), pericardium,
- Phrenic nerve, azygos vein[d], thoracic nerve roots (i.e., T1, T2), stellate ganglion or
- Separate tumour nodule(s) in the same lobe as the primary

cT4 Tumour more than 7 cm or
Tumour of any size that invades any of the following:
- Mediastinum, thymus, trachea, carina,
- Recurrent laryngeal nerve, vagus nerve,
- Oesophagus, diaphragm,
- Heart, aorta, superior or inferior vena cava, intrapericardial pulmonary arteries or veins, supra-aortic arteries, brachiocephalic veins, subclavian vessels,
- Vertebral body, lamina, spinal canal, cervical nerve roots, brachial plexus or separate tumour nodule(s) in a different ipsilateral lobe to that of the primary

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed

cN0 No regional lymph node metastasis

cN1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and/or intrapulmonary nodes, including involvement by direct extension

cN2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node station(s)
- cN2a Metastasis in a single station
- cN2b Metastasis in multiple ipsilateral stations

cN3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

M – Distant Metastasis

cM0 No distant metastasis

cM1 Distant metastasis

- cM1a Separate tumour nodule(s) in a contralateral lobe, tumour with pleural or pericardial nodules or malignant pleural or pericardial effusion[e]
- cM1b Single extrathoracic metastasis in a single organ or organ system[f]
- cM1c Multiple extrathoracic metastases in a single or multiple organ(s) or organ system(s)
  - M1c1 Multiple extrathoracic metastases in a single organ or organ system
  - M1c2 Multiple extrathoracic metastases in multiple organs or organ systems(s)

Notes

[a] Tis includes adenocarcinoma in situ – Tis(AIS) – and squamous carcinoma in situ – Tis (SCIS).

[b] The uncommon superficial spreading tumour of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified as T1a.

[c] Solitary adenocarcinoma (not more than 3 cm in greatest dimension), with a predominantly lepidic pattern and not more than 5 mm invasion in greatest dimension in any one focus. Invasive mucinous adenocarcinomas should be staged as other invasive adenocarcinomas, i.e., only the invasive size being used as the T descriptor (regardless of the extent of the lepidic component).

[d] Although these structures lie within the mediastinum invasion of these structure is not considered sufficient mediastinal penetration to be classified as a T4 category.

[e] Most pleural (pericardial) effusions with lung cancer are due to the tumour. In a few patients, however, multiple microscopic examinations of pleural (pericardial) fluid are negative for tumour, and the fluid is non-bloody and is not an exudate. Where these elements and clinical judgment dictate that the effusion is not related to the tumour, the effusion should be excluded as a staging descriptor.

[f] This includes the involvement of a single non-regional node.

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of hilar and mediastinal lymphadenectomy specimen(s) should ordinarily include six or more lymph node stations. Three of these stations should be mediastinal, including the subcarinal, and three from N1 stations. Labelling according to the IASLC chart and table of definitions given is desirable (reference).[1] If all the lymph nodes examined are negative, but the number of stations ordinarily examined is not met, classify as pN0.

Stage

Occult carcinoma	TX	N0	M0
Stage 0	Tis	N0	M0
Stage IA1	T1mi	N0	M0
	T1a	N0	M0
Stage IA2	T1b	N0	M0
Stage IA3	T1c	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T1	N1	M0
	T2b	N0	M0
Stage IIB	T1	N2a	M0
	T2	N1	M0
	T3	N0	M0
Stage IIIA	T1	N2b	M0
	T2	N2a	M0
	T3	N1, N2a	M0
	T4	N0, N1	M0
Stage IIIB	T1	N3	M0
	T2	N2b, N3	M0
	T3	N2b	M0
	T4	N2a,b	M0
Stage IIIC	T3,4	N3	M0
Stage IVA	Any T	Any N	M1a, M1b
Stage IVB	Any T	Any N	M1c1, M1c2

Prognostic Factors Grid – Non-Small-Cell Lung Carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Oligometastatic disease Number of metastatic sites Brain metastases Pleural and lymphovascular invasion R status EGFR, ALK gene expression	Performance status Comorbidities Tobacco use	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Grade Spread through air spaces (STAS) PDL1, KRAS.	Sex	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information Education level Marital status R status after surgery

Prognostic Factors Grid – Small-Cell Lung Carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Site of metastases (Brain)	Age Sex Performance status Comorbidity	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	LDH Alkaline phosphatase Paraneoplastic syndrome Metastatic site – brain vs liver Number of metastatic sites		Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.
Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang.

Pleural Mesothelioma
(ICD-O-4 C38.4)

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies only to mesothelioma of the pleura.

Changes in this edition from the eighth edition are based on recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project (references).[7–10]

There should be histological confirmation of the disease.

Regional Lymph Nodes

The regional lymph nodes are the intrathoracic, internal mammary, scalene and supraclavicular nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour limited to the ipsilateral pleura and no involvement of the fissure: Psum ≤12 mm* and Fmax ≤5 mm**

cT2 Tumour limited to the ipsilateral pleura: Psum ≤12 mm*
with involvement of any of the following:
Fissure – Fmax > 5 mm
Mediastinal fat invasion
Solitary area of chest wall soft tissue invasion
or
Tumour limited to the ipsilateral pleura, with Psum > 12 mm ≤ 30 mm*

with or without involvement of the following:
Fissure – Fmax > 5 mm
Mediastinal fat invasion
Solitary area of chest wall soft tissue invasion

cT3 Tumour limited to ipsilateral pleura: with Psum > 30 mm*
with or without involvement of the following:
Fissure – Fmax > 5 mm
Mediastinal fat invasion
Solitary area of chest wall soft tissue invasion

cT4 Tumour involves any of the following:
- Diffuse chest wall soft tissue involvement
- Chest wall with rib involvement.
- Mediastinal organs (oesophagus, trachea, heart, great vessels, spine)
- Direct extension through the diaphragm or pericardium
- Direct extension to contralateral pleura
- Malignant pericardial effusion

Notes

* As measured on CT scan.

Psum = sum of maximal pleural thickness. Measurements are made on axial images perpendicular to the chest wall or mediastinum in the area of estimated maximal pleural thickness in each third of the hemithorax (pmax1, pmax2 and pmax3) and combined to estimate the total pleural thickness (*Psum= pmax1+pmax2+pmax3*).

Fmax = maximal pleural thickness along the fissures.

See Figure 2.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastases to ipsilateral intrathoracic lymph nodes (includes ipsilateral bronchopulmonary, hilar, subcarinal, paratracheal, aortopulmonary, paraesophageal, peridiaphragmatic, pericardial fat pad or intercostal and internal mammary nodes)
cN2 Metastases to contralateral intrathoracic lymph nodes and/or
Metastases to ipsilateral or contralateral supraclavicular lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

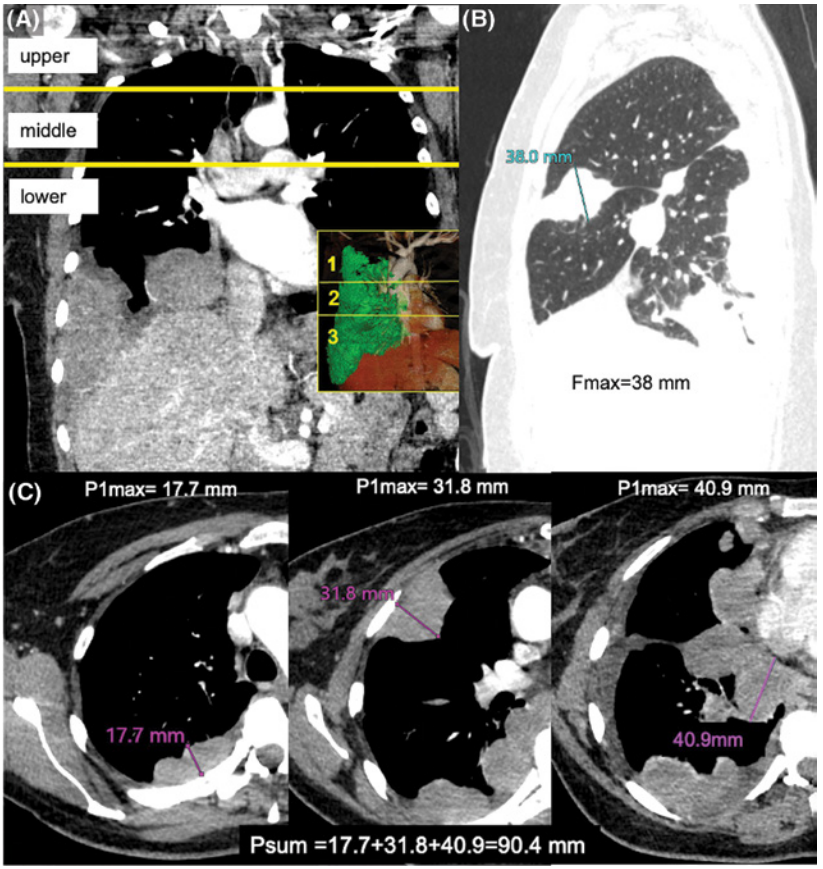


Figure 2 (A) Coronal and sagittal images of patients with pleural mesothelioma illustrating division of the chest into approximate thirds by a line drawn at the level of the aortic arch and a second line at the top of the left atrium, dividing the chest into three relatively equal parts of upper, middle and lower levels. The maximum pleural thickness on each of these levels (pmax1, pmax2 and pmax3) is measured and combined to derive a sum of maximum pleural thickness (Psum = pmax1 + pmax2 + pmax3). (B) Sagittal image revealing fissure involvement by tumour; maximal fissure thickness Fmax = 38 mm. (C) Axial images with maximal pleural thickness measurement at each of the three levels: p1max = 17.7 mm, p2max = 31.8 mm, and p3max = 40.9 mm, and Psum = 17.7 + 31.8 + 40.9 = 90.4 mm. Source: Gill et al.[8]/with permission of Elsevier.

pTNM Pathological Classification

pT – Primary Tumour

pT1 Tumour limited to the ipsilateral pleura and no involvement of the fissure

pT2 Tumour limited to the ipsilateral pleura with any of the following:
- the fissure
- ipsilateral lung parenchyma
- non-transmural diaphragm involvement

pT3 Tumour limited to ipsilateral pleura with or without fissure involvement and with invasion of any of the following:
- mediastinal fat
- surface of the pericardium
- endothoracic fascia
- solitary area of chest wall soft tissue involvement

pT4 Tumour involves any of the following:
- diffuse chest wall soft tissue involvement
- chest wall with rib involvement.
- mediastinal organs (oesophagus, trachea, heart, great vessels, spine)
- direct extension through the diaphragm or pericardium
- direct extension to contralateral pleura
- malignant pericardial effusion

The pN categories correspond to the cN categories. For pM, see page 8.

Stage – Pleural Mesothelioma

Stage I	T1	N0	M0
Stage II	T1	N1	M0
	T2	N0	M0
Stage IIIA	T1	N2	M0
	T2	N1,2	M0
	T3	Any N	M0
Stage IIIB	T4	Any N	M0
Stage IV	Any T	Any N	M1

Thymus Tumours
(ICD-O-4 C37.9)

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies to epithelial tumours of the thymus, including thymomas, thymic carcinomas and neuroendocrine tumours of the thymus. It does not apply to sarcomas, lymphomas and other rare tumours.

Changes in this edition from the eighth edition are based on recommendations from the International Association for the Study of Lung Cancer (IASLC) Staging Project (references). [11–13]

There should be confirmation of the disease and division of cases by histological type.

Regional Lymph Nodes

The regional lymph nodes are the anterior (perithymic) lymph nodes, the deep intrathoracic lymph nodes and the cervical lymph nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour limited to the thymus, with or without encapsulation, or directly invades the mediastinal pleura but does not involve any other mediastinal structure.
- cT1a 5 cm or less in its greatest dimension.
- cT1b larger than 5 cm in its greatest dimension.

cT2 Tumour with direct involvement of the pericardium (partial or full thickness), the lung or the phrenic nerve.

cT3 Tumour directly invades any of the following: the brachiocephalic vein, the superior vena cava, the chest wall or extrapericardial pulmonary arteries or veins

cT4 Tumour with direct invasion into any of the aorta (ascending, arch, or descending), arch vessels, intrapericardial pulmonary artery or veins, the myocardium, the trachea or the oesophagus

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in anterior (perithymic) lymph nodes
cN2 Metastasis in deep intrathoracic or cervical lymph nodes, including the paratracheal, subcarinal, aortopulmonary window, hilar, jugular and supraclavicular nodes

M – Distant Metastasis

cM0 No metastasis
cM1 Distant metastasis
  cM1a Separate pleural or pericardial nodule(s)
  cM1b Pulmonary intraparenchymal nodule(s) or distant metastases.

TNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage –Thymic Tumours

Stage I	T1a,b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T4	N0	M0
Stage IVA	Any T	N1	M0
	Any T	N0, N1	M1a
Stage IVB	Any T	N2	M0, M1a
	Any T	Any N	M1b

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Tumours of Bone and Soft Tissues

Introductory Notes

The following staging systems are included:

- Bone
- Soft tissues
- Gastrointestinal stromal tumours

G Histopathological Grading

The grading of bone and soft tissue sarcomas is based on a three-tiered grade classification. In this classification, Grade 1 is considered 'low grade' and Grades 2 and 3 'high grade'.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Bone
(ICD-O-4 C40, 41)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to all primary malignant bone tumours except lymphoma, plasmacytoma, plasma cell myeloma/multiple myeloma, surface/juxtacortical osteosarcoma and juxtacortical chondrosarcoma. There should be histological confirmation of the disease and division of cases by histological type and grade.

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. Regional node involvement is rare, and cases in which nodal status is not assessed either clinically or pathologically could be considered N0 instead of NX or pNX.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

Appendicular Skeleton, Trunk, Skull and Facial Bones

cT1 Tumour 8 cm or less in greatest dimension
cT2 Tumour more than 8 cm in greatest dimension
cT3 Discontinuous tumours in the primary bone site

Spine

cT1 Tumour confined to a single vertebral segment or two adjacent vertebral segments
cT2 Tumour confined to three adjacent vertebral segments
cT3 Tumour confined to four adjacent vertebral segments
cT4a Tumour invades into the spinal canal
cT4b Tumour invades the adjacent vessels or tumour thrombosis within the adjacent vessels

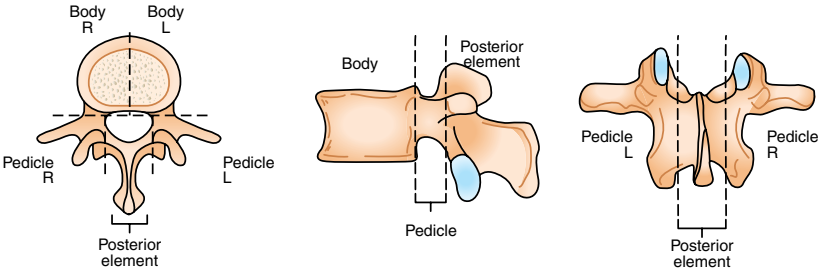

Figure 1 The five vertebral segments: right pedicle, right body, left body, left pedicle, and posterior element. Source: Adapted from AJCC Cancer Staging Manual 2017 © Springer Nature.

Pelvis

cT1a A tumour 8 cm or less in size and confined to a single pelvic segment with no extraosseous extension

cT1b A tumour greater than 8 cm in size and confined to a single pelvic segment with no extraosseous extension

cT2a A tumour 8 cm or less in size and confined to a single pelvic segment with extraosseous extension or confined to two adjacent pelvic segments without extraosseous extension

cT2b A tumour greater than 8 cm in size and confined to a single pelvic segment with extraosseous extension or confined to two adjacent pelvic segments without extraosseous extension

cT3a A tumour 8 cm or less in size and confined to two pelvic segments with extraosseous extension

cT3b A tumour greater than 8 cm in size and confined to two pelvic segment with extraosseous extension

cT4a Tumour involving three adjacent pelvic segments or crossing the sacroiliac joint to the sacral neuroforamen

cT4b Tumour encasing the external iliac vessels or gross tumour thrombus in major pelvic vessels

Note

The four pelvic segments are:

Sacrum lateral to the sacral foramen
Iliac wing
Acetabulum/periacetabulum
Pelvic rami, symphysis and ischium.

See Figure 2.

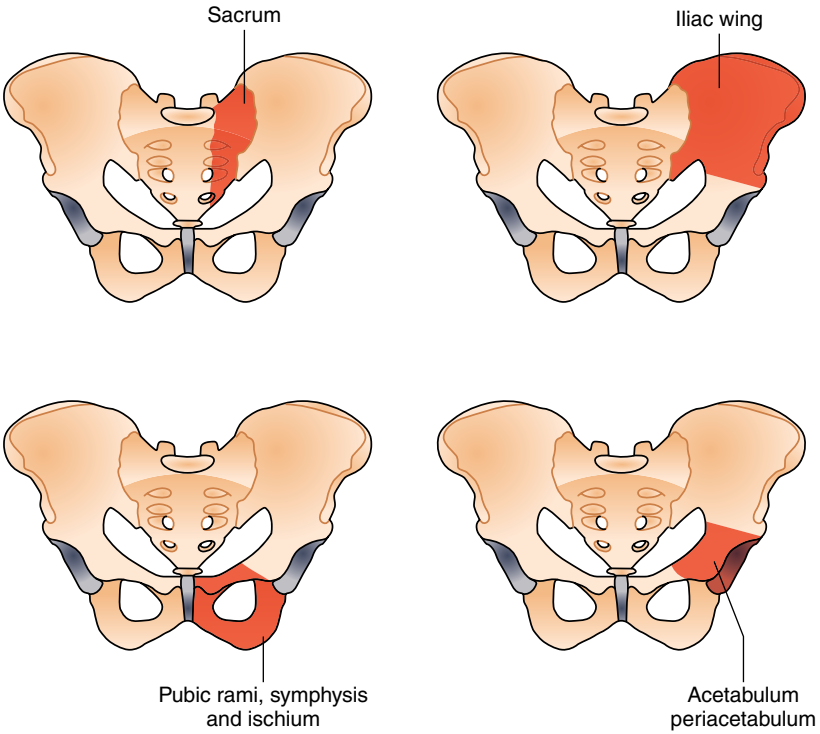

Figure 2 The four pelvic segments: sacrum segment, iliac wing segment, pubic rami, symphysis and ischium segment and acetabulum, periacetabulum segment. Source: Adapted from AJCC Cancer Staging Manual 2017 © Springer Nature.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
M1a Lung
M1b Other distant sites

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage – Appendicular Skeleton, Trunk, Skull and Facial Bones

Stage IA	T1	N0	M0	G1, GX low grade
Stage IB	T2, T3	N0	M0	G1, GX low grade
Stage IIA	T1	N0	M0	G2, G3 high grade
Stage IIB	T2	N0	M0	G2, G3 high grade
Stage III	T3	N0	M0	G2, G3 high grade
Stage IVA	Any T	N0	M1a	Any G
Stage IVB	Any T	N1	Any M	Any G
	Any T	Any N	M1b	Any G

Stage – Spine and Pelvis

There is no stage for bone sarcomas of the spine or pelvis.

Soft Tissues
(ICD-O-4 C15-C26, C34-C37, C38.1-3, C47-C49, C51-C53, C58, C60-C68)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification only applies to malignant and uncertain behaviour mesenchymal tumours with metastatic potential (including sarcomas). There should be histological confirmation of the disease and division of cases by histological type and grade.

Anatomical Sites

1. Connective, subcutaneous and other soft tissues (C49); peripheral nerves (C47)
2. Retroperitoneum (C48.0)
3. Mediastinum: anterior (C38.1); posterior (C38.2); mediastinum, NOS (C38.3).

Histological Types of Tumour

The following histological types are not included:

- Kaposi sarcoma
- Dermatofibrosarcoma (protuberans)
- Fibromatosis (desmoid tumour)
- Sarcoma arising from the dura mater and brain
- Angiosarcoma, an aggressive sarcoma, is excluded because its natural history is not consistent with the classification.

For tumours in paediatric patients, please see page 242.

Note

Malignant phyllodes tumour is staged as a soft tissue sarcoma of the superficial trunk.

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. Regional node involvement is rare, and cases in which nodal status is not assessed either clinically or pathologically could be considered N0 instead of cNX or pNX.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

Extremity and Superficial Trunk

cT1 Tumour 5 cm or less in greatest dimension
cT2 Tumour more than 5 cm but not more than 10 cm in greatest dimension
cT3 Tumour more than 10 cm but not more than 15 cm in greatest dimension
cT4 Tumour more than 15 cm in greatest dimension

Retroperitoneum

cT1 Tumour 5 cm or less in greatest dimension
cT2 Tumour more than 5 cm but not more than 10 cm in greatest dimension
cT3 Tumour more than 10 cm but not more than 15 cm in greatest dimension
cT4 Tumour more than 15 cm in greatest dimension

Head and Neck

cT1 Tumour 2 cm or less in greatest dimension
cT2 Tumour more than 2 cm but not more than 4 cm in greatest
cT3 Tumour more than 4 cm in greatest dimension
cT4a Tumour invades the orbit, skull base or dura, central compartment viscera, facial skeleton and or pterygoid muscles
cT4b Tumour invades the brain parenchyma, encases the carotid artery, invades prevertebral muscle or involves the central nervous system by perineural spread

Thoracic and Abdominal Viscera

cT1 Tumour confined to a single organ
cT2a Tumour invades serosa or visceral peritoneum
cT2b Tumour with microscopic extension beyond the serosa
cT3 Tumour invades another organ or macroscopic extension beyond the serosa
cT4a Multifocal tumour involving not more than two sites in one organ
cT4b Multifocal tumour involving more than two sites but not more than five sites
cT4c Multifocal tumour involving more than five sites

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage – Extremity and Superficial Trunk and Retroperitoneum

Stage IA	T1	N0	M0	G1, GX low grade
Stage IB	T2, T3, T4	N0	M0	G1, GX low grade
Stage II	T1	N0	M0	G2, G3 high grade
Stage IIIA	T2	N0	M0	G2, G3 high grade
Stage IIIB	T3, T4	N0	M0	G2, G3 high grade
Stage IIIB	Any T	N1*	M0	Any G
Stage IV	Any T	Any N	M1	Any G

Note

* AJCC classifies N1 as stage IV for extremity and superficial trunk.

Stage – Head and Neck and Thoracic and Abdominal Viscera

There is no stage for soft tissue sarcoma of the head and neck and thoracic and abdominal viscera.

Gastrointestinal Stromal Tumour (GIST)
(ICD-O-4 C15-20, C48.1-2)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to gastrointestinal stromal tumours. There should be histological confirmation of the disease.

Anatomical Sites and Subsites

- Oesophagus (C15)
- Stomach (C16)
- Small intestine (C17)
  1. Duodenum (C17.0)
  2. Jejunum (C17.1)
  3. Ileum (C17.2)
- Colon (C18)
- Rectosigmoid junction (C19)
- Rectum (C20)
- Omentum (C48.1)
- Mesentery (C48.1)

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour; see gastrointestinal sites for details.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence for primary tumour

cT1 Tumour 2 cm or less
cT2 Tumour more than 2 cm but not more than 5 cm
cT3 Tumour more than 5 cm but not more than 10 cm
cT4 Tumour more than 10 cm in greatest dimension

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed*
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

Note

* NX: Regional lymph node involvement is rare for GISTs, so that cases in which the nodal status is not assessed clinically or pathologically could be considered N0 instead of NX or pNX.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

G Histopathological Grading

Grading for GIST is dependent on the mitotic rate
Low mitotic rate: 5 or fewer per 5 mm^2
High mitotic rate: over 5 per 5 mm^2

Stage

Staging criteria for gastric tumours can be applied in primary, solitary omental GISTs. Staging criteria for intestinal tumours can be applied to GISTs in less common sites, such as oesophagus, colon, rectum and mesentery.

Gastric GIST (including primary omental)

				Mitotic rate
Stage IA	T1, T2	N0	M0	Low
Stage IB	T3	N0	M0	Low
Stage II	T1, T2	N0	M0	High
	T4	N0	M0	Low
Stage IIIA	T3	N0	M0	High
Stage IIIB	T4	N0	M0	High
Stage IV	Any T	N1	M0	Any rate
	Any T	Any N	M1	Any rate

Non Gastric (small intestine and other sites) GIST

				Mitotic rate
Stage I	T1, T2	N0	M0	Low
Stage II	T3	N0	M0	Low
Stage IIIA	T1	N0	M0	High
	T4	N0	M0	Low
Stage IIIB	T2, T3, T4	N0	M0	High
Stage IV	Any T	N1	M0	Any rate
	Any T	Any N	M1	Any rate

Prognostic Factors Grid

Prognostic factors for bone sarcomas

Prognostic factors	Tumour related	Host related	Environment related
Essential	TNM Anatomical site Histological type Volume of tumour: Depth of invasion Grade (well to poorly differentiated) Mitotic rate Alkaline phosphatase and lactate dehydrogenase (LDH) Site of metastases Pathological fracture Tumour response to neoadjuvant chemotherapy	Age Performance status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education Resection margin Residual disease after resection
Additional	*EWS–FL11* fusion transcript for Ewing sarcoma	Germline TP53	Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

Prognostic factors for soft tissue sarcomas

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Anatomical site Histological type Depth of invasion Grade (well to poorly differentiated) Mitotic rate for GIST Alkaline phosphatase and lactate dehydrogenase – LDH (Ewing's)	Age Performance status	Distance from treatment centre Access to affordable health services of decent quality including specific investigations and/or treatments Socioeconomic status Education. Resection margin
Additional	Neurovascular invasion Bone invasion Presence of *c-Kit* mutation for GIST Mutational site in *c-Kit* or *PDGFRA* gene for GIST *EWS–FL11* fusion transcript for Ewing sarcoma *SYT–SSX* fusion transcript for synovial sarcoma *FOXO1* translocation for alveolar rhabdomyosarcoma Surgical resection margins Presentation status (primary vs recurrence) NTRK gene fusion Germline TP53 (Li–Fraumeni syndrome)	Neurofibromatosis (NF1) Radiation-induced sarcomas Age Germline TP53	Expertise of a treatment at the specific level (surgery, medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Skin Tumours

Introductory Notes

The classifications apply to carcinomas of the skin* [excluding vulva (see page 160), penis (see page 184) and perianal skin (see page 79)], melanomas of the skin, including eyelid, and to Merkel cell carcinoma.

Anatomical Sites

The following sites are identified by ICD-O-4 topography rubrics:

- Lip including vermillion border and commissure (C00.0-2, C00.6, C44.0)
- Eyelid (C44.1)
- External ear (C44.2)
- Other and unspecified parts of face (C44.3)
- Scalp and neck (C44.4)
- Trunk excluding anal margin and perianal skin (C44.5)
- Upper limb and shoulder (C44.6)
- Lower limb and hip (C44.7)
- Scrotum (C63.2)

In addition, for melanoma and Merkel cell carcinomas, the following sites are identified by ICD-O-4 topography rubrics:

- Perianal skin (C21.3)
- Labium majus (C51.0)
- Labium minus (C51.1)
- Clitoris (C51.2)
- Overlapping lesions (C51.8)
- Vulva, NOS (C51.9)
- Prepuce (C60.0)
- Glans penis (C60.1)
- Body of penis (60.2)
- Overlapping lesions of penis (C60.8)
- Penis, NOS (60.9)

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour.

Unilateral Tumours

- **Head, neck:** Ipsilateral preauricular, submandibular, cervical and supraclavicular lymph nodes
- **Thorax:** Ipsilateral axillary lymph nodes
- **Upper limb:** Ipsilateral epitrochlear and axillary lymph nodes
- **Abdomen, loins and buttocks:** Ipsilateral inguinal lymph nodes
- **Lower limb:** Ipsilateral popliteal and inguinal lymph nodes

Tumours in the Boundary Zones Between these sites

The lymph nodes pertaining to the regions on both sides of the boundary zone are considered to be the regional lymph nodes.

The following 4-cm wide bands are considered as boundary zones:

Between	Along
Right/left	Midline
Head and neck/thorax	Clavicula–acromion–upper shoulder blade edge
Thorax/upper limb	Shoulder–axilla–shoulder
Thorax/abdomen, loins and buttocks	*Front:* middle between navel and costal arch; *Back:* lower border of thoracic vertebrae (midtransverse axis)
Abdomen, loins and buttock/lower limb	Groin–trochanter–gluteal sulcus

Any metastasis to other than the listed regional lymph nodes is considered as M1.

Carcinoma of Skin (excluding eyelid, head and neck, perianal, vulva and penis)
(ICD-O-4 C44.5-7, C63.2)*

Rules for Classification*

The classification applies only to carcinomas, excluding Merkel cell carcinoma. There should be histological confirmation of the disease and division of cases by histological type.

Note

* The AJCC only includes the classification for skin carcinoma of the head and neck.

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 134.

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be identified
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cT1	Tumour 2 cm or less in greatest dimension
cT2	Tumour >2 cm and ≤4 cm in greatest dimension
cT3	Tumour >4 cm in greatest dimension or minor bone erosion or perineural invasion or deep invasion*
cT4a	Tumour with gross cortical bone/marrow invasion
cT4b	Tumour with axial skeleton invasion including foraminal involvement and/or vertebral foramen involvement to the epidural space

Notes

* Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumour).

Perineural invasion is defined as tumour cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in caliber or involvement of five or more nerves per section,[1] without foramen or skull base invasion or transgression.

In the case of multiple simultaneous tumours, the tumour with the highest T category is classified and the number of separate tumours is indicated in parentheses, e.g., T2(5).

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single lymph node 3 cm or less in greatest dimension
cN2 Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral nodes not more than 6 cm in greatest dimension
cN3 Metastasis in a lymph node more than 6 cm in greatest dimension

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastatic disease*

Note

* Contralateral nodes in non-melanoma non-head and neck cancer are distant metastases.

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

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

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T1, T2, T3	N2, N3	M0
	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Prognostic Factors Grid – Non-Melanoma/Merkel Cell Skin

Tumour-, host- and environment-related prognostic factors for skin cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Histopathological type Location Thickness PNI, size of nerves involved >0.01 mm PNI, number of nerves involved	Age Performance status Immune suppression Recurrent disease	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status Smoking history
Additional	Tumour borders Differentiation Rate of growth LVSI	Genetic factors Gorlin syndrome Chronic inflammation, scars, burns	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information Margin status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Massey PR, Wang David M, Murad F, et al. Extensive perineural invasion vs nerve caliber to assess cutaneous squamous cell carcinoma prognosis. *JAMA Dermatol* 2023; 159(12): 1332–1338. doi:https://doi.org/10.1001/jamadermatol.2023.3703.

Carcinoma of Skin of the Head and Neck Region
(ICD-O-4 C00.0-2, C00.6, C44.0, C44.2-4)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to cutaneous carcinomas of the head and neck region, excluding the eyelid and excluding Merkel cell carcinoma and melanoma. There should be histological confirmation of the disease.

Anatomical Sites

The following sites are identified by ICD-O-3 topography rubrics:

- Lip including vermillion border and commissure (C00.0-2, C00.6, C44.0). For mucosal lip, see page 18
- External ear (C44.2)
- Other and unspecified parts of face (C44.3)
- Scalp and neck (C44.4).

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be identified
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cT1	Tumour 2 cm or less in greatest dimension
cT2	Tumour >2 cm and ≤4 cm in greatest dimension
cT3	Tumour >4 cm in greatest dimension or minor bone erosion or perineural invasion or deep invasion[1]
cT4a	Tumour with gross cortical bone/marrow invasion
cT4b	Tumour with foraminal involvement of the axial skeleton[2] invasion with foraminal involvement or invasion into the epidural space

Notes

[1] Deep invasion is defined as invasion beyond the subcutaneous fat or >6 mm (as measured from the granular layer of adjacent normal epidermis to the base of the tumour). Perineural invasion is defined as tumour cells within the nerve sheath of a nerve lying deeper than the dermis or measuring 0.1 mm or larger in calibre or involvement of five or more nerves per section, without foramen or skull base invasion or transgression.

[2] Axial skeleton includes the skull, vertebrae and sacrum.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed.
cN0 No regional lymph node metastasis
cN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
cN2 Metastasis described as:
- cN2a Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension
- cN2b Metastasis in multiple ipsilateral lymph nodes, not more than 6 cm in greatest dimension, without extranodal extension
- cN2c Metastasis in bilateral or contralateral lymph nodes, not more than 6 cm in greatest dimension, without extranodal extension

cN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension
cN3b Metastasis in a single or multiple lymph nodes with clinical extranodal extension*

Note

* Clinical extranodal extension is defined as the presence of skin involvement or soft tissue invasion with deep fixation to underlying muscle or adjacent anatomical structures or clinical signs of nerve involvement. Image detected unequivocal extranodal extension is becoming standard.

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the clinical cT categories. For pM, see page 8.

pN – Regional Lymph Nodes

Histological examination of a selective neck dissection specimen should ordinarily include 10 or more lymph nodes. Histological examination of a radical or modified radical neck dissection specimen should ordinarily include 15 or more lymph nodes.

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension without extranodal extension
pN2 Metastasis described as:
- pN2a Metastasis in a single ipsilateral lymph node, less than 3 cm in greatest dimension with extranodal extension or, more than 3 cm but not more than 6 cm in greatest dimension without extranodal extension

pN2b Metastasis in multiple ipsilateral lymph nodes, not more than 6 cm in greatest dimension, without extranodal extension

pN2c Metastasis in bilateral or contralateral lymph nodes, not more than 6 cm in greatest dimension, without extranodal extension

pN3a Metastasis in a lymph node more than 6 cm in greatest dimension without extranodal extension

pN3b Metastasis in a lymph node more than 3 cm in greatest dimension with extranodal extension or multiple ipsilateral, or any contralateral or bilateral node(s) with extranodal extension

Note

* Reference

Massey PR, Wang David M, Murad F, et al. Extensive perineural invasion vs nerve caliber to assess cutaneous squamous cell carcinoma prognosis. *JAMA Dermatol* 2023; 159(12): 1332–1338.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T1, T2, T3	N2, N3	M0
	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Carcinoma of Skin of the Eyelid
(ICD-O-4 C44.1)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules of Classification

There should be histological confirmation of the disease and division of cases by histological type, for example, basal cell, squamous cell and sebaceous carcinoma. Melanoma of the eyelid is classified with melanoma of the skin, see page 144.

Regional Lymph Nodes

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

TNM Clinical Classification

cT – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ

cT1 Tumour 10 mm or less in greatest dimension
- cT1a Not invading the tarsal plate or eyelid margin
- cT1b Invades tarsal plate or eyelid margin
- cT1c Involves full thickness of eyelid

cT2 Tumour >10 mm, but 20 mm or less in greatest dimension
- cT2a Not invading the tarsal plate or eyelid margin
- cT2b Invades the tarsal plate or eyelid margin
- cT2c Involves full thickness of eyelid

cT3 Tumour >20 mm in greatest dimension
- cT3a Not invading the tarsal plate or eyelid margin
- cT3b Invades tarsal plate or eyelid margin
- cT3c Involves full thickness of eyelid

cT4 Any eyelid tumour that invades adjacent ocular or orbital or facial structures
- cT4a Tumour invades ocular or intraorbital structures
- cT4b Tumour invades (or erodes through) the bony walls of orbit or extends to paranasal sinuses or invades the lacrimal sac/nasolacrimal duct or brain

cN – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No evidence of lymph node involvement
cN1 Metastasis in a single ipsilateral regional lymph node, 3 cm or less in greatest dimension
cN2 Metastasis in a single ipsilateral lymph node more than 3 cm in greatest dimension or in bilateral or contralateral lymph nodes or multiple ipsilateral lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T2b, T2c, T3	N0	M0
Stage IIB	T4	N0	M0
Stage IIIA	Any T	N1	M0
Stage IIIB	Any T	N2	M0
Stage IV	Any T	Any N	M1

Prognostic Factor Grid – Eyelid

Prognostic factors for survival for eyelid cancers

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Location (worse prognosis if tumour involves the orbit or sinus)	Immunosuppression Preauricular and/or cervical lymph node involvement Systemic metastatic disease at presentation	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status

(*Continued*)

Prognostic factors	Tumour related	Host related	Environment related*
Additional	BCC: nodular better than morpheaform type Sebaceous tumours have a worse prognosis than BCC or SCC		Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R Status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Melanoma of Skin
(ICD-O-4 C00.0-2, C00.6, C21.3, C44, C51, C60, C63.2)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

There should be histological confirmation of the disease.

The following are the procedures for assessing N and M categories:

N categories Physical examination and imaging
M categories Physical examination and imaging

When patients present with multiple primary melanomas, each different anatomical site of the skin is considered a different primary.

The classifications applies to melanomas of the skin, including vulva, penis and perianal skin, but excludes melanomas of the upper aerodigestive tract (see page 49).

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 134.

TNM Clinical Classification

T – Primary Tumour

The extent of the tumour is classified after excision, see pT, page 145.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in one regional lymph node or intralymphatic regional metastasis *without* nodal metastases
- cN1a Only microscopic metastasis (clinically occult)
- cN1b Macroscopic metastasis (clinically apparent)
- cN1c Satellite or in-transit metastasis *without* regional nodal metastasis

cN2 Metastasis in two or three regional lymph nodes or satellite or in-transit metastasis *with* lymph node metastases
- cN2a Metastasis in two or three regional lymph nodes, with only microscopic nodal metastasis
- cN2b Metastasis in two or three regional lymph nodes, clinically detected in at least one node

cN2c Satellite or in-transit metastasis *with* only one regional nodal metastasis, (microscopic or clinical)

cN3 Metastasis in four or more regional lymph nodes, or matted metastatic regional lymph nodes, or satellite(s) or in-transit metastasis *with* metastasis in two or more regional lymph node(s)

- cN3a Metastasis in four or more regional lymph nodes with only microscopic nodal metastasis
- cN3b Metastasis in four or more regional lymph nodes clinically detected in at least one node, or two or more matted nodes.
- cN3c Satellite(s) or in-transit metastasis either with two or more regional nodal metastasis (microscopic or clinical) or two or more matted nodes.

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis*

- M1a Skin, subcutaneous tissue or lymph node(s) beyond the regional lymph nodes
- M1b Lung
- M1c Other non-central nervous system sites
- M1d Central nervous system

Notes

* Suffixes for M category:

(0) lactic dehydrogenase (LDH) – not elevated

(1) LDH – elevated

so that M1a(1) is metastasis in skin, subcutaneous tissue, or lymph node(s) beyond the regional lymph nodes with elevated LDH.

No suffix is used if LDH is not recorded or unspecified.

pTNM Pathological Classification

pT – Primary Tumour

pTX Primary tumour cannot be assessed*

pT0 No evidence of primary tumour or regressed melanomas

pTis Melanoma in situ (Clark level I)

Note

* pTX includes shave biopsies and curettage that do not fully assess the thickness of the primary.

pT1 Tumour 1 mm or less in thickness*

- pT1a less than 0.8 mm in thickness without ulceration
- pT1b less than 0.8 mm in thickness with ulceration or 0.8 mm or more, but not more than 1 mm in thickness, with or without ulceration

pT2 Tumour more than 1 mm, but not more than 2 mm in thickness
- pT2a without ulceration
- pT2b with ulceration

pT3 Tumour more than 2 mm, but not more than 4 mm in thickness
- pT3a without ulceration
- pT3b with ulceration

pT4 Tumour more than 4 mm in thickness
- pT4a without ulceration
- pT4b with ulceration

Note

* Tumour thickness measurements are *rounded* to the nearest 0.1 mm before the T category is assigned.

pN – Regional Lymph Nodes

The pN categories correspond to the N categories.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0. Classification based solely on sentinel node biopsy without subsequent axillary lymph node dissection is designated (sn) for sentinel nodes, e.g., (p)N1(sn). (See Introduction, page 7.)

pM – Distant Metastasis

For pM, see page 8.

Clinical Stage

Stage 0	Tis	N0	cM0
Stage IA	T1a	N0	cM0
Stage IB	T1b	N0	cM0
	T2a	N0	cM0
Stage IIA	T2b	N0	cM0
	T3a	N0	cM0
Stage IIB	T3b	N0	cM0
	T4a	N0	cM0
Stage IIC	T4b	N0	cM0
Stage III	Any T	N1, N2, N3	cM0
Stage IV	Any T	Any N	cM1

Pathological Stage*

Stage 0	pTis	c/pN0	cM0
Stage I	pT1	c/pN0	cM0
Stage IA	pT1a	c/pN0	cM0
	pT1b	c/pN0	cM0
Stage IB	pT2a	pN0	cM0
Stage IIA	pT2b	pN0	cM0
	pT3a	pN0	cM0
Stage IIB	pT3b	pN0	cM0
	pT4a	pN0	cM0
Stage IIC	pT4b	pN0	cM0
Stage III	Any pT	pN1, pN2, pN3	cM0
Stage IIIA	pT1a, T1b, T2a	pN1a, pN2a	cM0
Stage IIIB	pT1a, T1b, T2a	pN1b, pN1c, pN2b	cM0
	pT2b–T3a	pN1, pN2a, pN2b,	cM0
Stage IIIC	pT1a, T1b, T2a, T2b, T3a	pN2c, pN3	cM0
	pT3b, T4a	N1, N2, N3	cM0
	pT4b	N1, N2	
Stage IIID	pT4b	N3	cM0
Stage IV	Any pT	Any N	M1

Note

* If lymph node(s) are identified with no apparent primary, the stage is as follows:

Stage IIIB	pT0	N1b, N1c	M0
Stage IIIC	pT0	N2b, N2c, N3b, N3c	M0

Prognostic Factors Grid –Melanoma

Prognostic factors for melanoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Tumour thickness Greatest tumour diameter Sentinel node burden Mitotic rate Ulceration Radial vs vertical growth Extent of metastatic disease LDH BRAF V600 mutation	Lymphocyte infiltrate Regression Age Gender Performance status Immunodeficiency Medication	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status Screening
Additional	Lymphovascular invasion Perineural invasion NRAS and KIT mutations	Site of primary Family history Medication	Expertise of a treatment at the specific level (surgery systemic therapy, immunotherapy) Access to information Sun exposure Tanning bed use

*** See page 12 for a more complete list of environmental and social determinants of health factors.**

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Merkel Cell Carcinoma of Skin
(ICD-O-4 C00, C44, C51, C60, C63.2, C80)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies only to Merkel cell carcinomas. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N and M categories:

T categories Physical examination
N categories Physical examination and imaging
M categories Physical examination and imaging

Regional Lymph Nodes

The regional lymph nodes are those appropriate to the site of the primary tumour. See page 134.

TNM Clinical Classification

T – Primary Tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension
T2 Tumour more than 2 cm, but not more than 5 cm in greatest dimension
T3 Tumour more than 5 cm in greatest dimension
T4 Tumour invades deep extradermal structures, i.e., cartilage, skeletal muscle, fascia or bone

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis
N2 In-transit metastasis *without* lymph node metastasis
N3 In-transit metastasis *with* lymph node metastasis

Note

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

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
- M1a Skin, subcutaneous tissues or non-regional lymph node(s)
- M1b Lung
- M1c Other site(s)

pTNM Pathological Classification

The pT category corresponds to the T category. For pM, see page 8.

pN0 Histological examination of a regional lymphadenectomy specimen will ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.
pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Regional lymph node metastasis
- pN1a(sn) Microscopic metastasis detected on sentinel node biopsy
- pN1a Microscopic metastasis detected on node dissection
- pN1b Macroscopic metastasis (clinically apparent)

pN2 In-transit metastasis *without* lymph node metastasis
pN3 In-transit metastasis *with* lymph node metastasis

Note

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

Clinical Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2, T3	N0	M0
Stage IIB	T4	N0	M0
Stage III	Any T	N1, N2, N3	M0
Stage IV	Any T	Any N	M1

Pathological Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T2, T3	N0	M0
Stage IIB	T4	N0	M0
Stage IIIA	T0	N1b	M0
	T1, T2, T3, T4	N1a, N1a(sn)	M0
Stage IIIB	T1, T2, T3, T4	N1b, N2, N3	M0
Stage IV	Any T	Any N	M1

Breast Tumours
(ICD-O-4 C50)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas and concerns the male as well as the female breast. There should be histological confirmation of the disease. The anatomical subsite of origin should be recorded but is not considered in classification.

In the case of multiple simultaneous primary tumours in one breast, the tumour with the highest T category should be used for classification. Simultaneous *bilateral* breast cancers should be classified independently to permit the division of cases by histological type.

Anatomical Subsites

1. Nipple (C50.0)
2. Central portion (C50.1)
3. Upper-inner quadrant (C50.2)
4. Lower-inner quadrant (C50.3)
5. Upper-outer quadrant (C50.4)
6. Lower-outer quadrant (C50.5)
7. Axillary tail (C50.6)

Regional Lymph Nodes

The regional lymph nodes are:

1. *Axillary* (ipsilateral): interpectoral (Rotter) nodes and lymph nodes along the axillary vein and its tributaries, which may be divided into the following levels:
   a) *Level I* (low-axilla): lymph nodes lateral to the lateral border of pectoralis minor muscle
   b) *Level II* (mid-axilla): lymph nodes between the medial and lateral borders of the pectoralis minor muscle and the interpectoral (Rotter) lymph nodes

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

c) *Level III* (apical axilla): apical lymph nodes and those medial to the medial margin of the pectoralis minor muscle, excluding those designated as subclavicular or infraclavicular

2. *Infraclavicular (subclavicular)* (ipsilateral)
3. *Internal mammary* (ipsilateral): lymph nodes in the intercostal spaces along the edge of the sternum in the endothoracic fascia
4. *Supraclavicular* (ipsilateral).

Note

Intramammary lymph nodes are coded as axillary lymph nodes level I. Any other lymph node metastasis is coded as a distant metastasis (M1), including cervical or contralateral internal mammary lymph nodes.

TNM Clinical Classification

T – Primary Tumour

cTX	Primary tumour cannot be assessed
cT0	No evidence of primary tumour
cTis	Carcinoma in situ
cTis (DCIS)	Ductal carcinoma in situ
cTis (LCIS)	Lobular carcinoma in situ[a]
cTis (Paget)	Paget disease of the nipple not associated with invasive carcinoma and/or carcinoma in situ (DCIS and/or LCIS) in the underlying breast parenchyma. Carcinomas in the breast parenchyma associated with Paget disease are categorised based on the size and characteristics of the parenchymal disease, although the presence of Paget disease should still be noted.
cT1	Tumour 2 cm or less in greatest dimension
	cT1mi Microinvasion 0.1 cm or less in greatest dimension[b]
	cT1a More than 0.1 cm but not more than 0.5 cm in greatest dimension
	cT1b More than 0.5 cm but not more than 1 cm in greatest dimension
	cT1c More than 1 cm but not more than 2 cm in greatest dimension
cT2	Tumour more than 2 cm but not more than 5 cm in greatest dimension
cT3	Tumour more than 5 cm in greatest dimension
cT4	Tumour of any size with direct extension to chest wall and/or to skin (ulceration or skin nodules)[c]
	cT4a Extension to chest wall (does not include pectoralis – muscle invasion only)
	cT4b Ulceration, ipsilateral satellite skin nodules or skin oedema (including peau d'orange)
	cT4c Both 4a and 4b
	cT4d Inflammatory carcinoma[d]

Notes

[a] The AJCC exclude Tis (LCIS).

[b] Microinvasion is the extension of cancer cells beyond the basement membrane into the adjacent tissues with no focus more than 0.1 cm in greatest dimension. When there are multiple foci of microinvasion, the size of only the largest focus is used to classify the microinvasion. (Do not use the sum of all individual foci.) The presence of multiple foci of microinvasion should be noted, as it is with multiple larger invasive carcinomas.

[c] Invasion of the dermis alone does not qualify as T4. Chest wall includes ribs, intercostal muscles and serratus anterior muscle but not pectoral muscle.

[d] Inflammatory carcinoma of the breast is characterised by diffuse, brawny induration of the skin with an erysipeloid edge, usually with no underlying mass. If the skin biopsy is negative and there is no localised measurable primary cancer, the T category is pTX when pathologically staging a clinical inflammatory carcinoma (T4d). Dimpling of the skin, nipple retraction or other skin changes, except those in T4b and T4d, may occur in T1, T2 or T3 without affecting the classification.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed (e.g., previously removed)
cN0 No regional lymph node metastasis
cN1 Metastasis in movable ipsilateral level I, II axillary lymph node(s)
cN2 Metastasis in ipsilateral level I, II axillary lymph node(s) that are clinically fixed or matted; or in clinically detected* ipsilateral internal mammary lymph node(s) in the *absence* of clinically evident axillary lymph node metastasis
- cN2a Metastasis in axillary lymph node(s) fixed to one another (matted) or to other structures
- cN2b Metastasis only in clinically detected* internal mammary lymph node(s) and in the *absence* of clinically detected axillary lymph node metastasis

cN3 Metastasis in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected* ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
- cN3a Metastasis in infraclavicular lymph node(s)
- cN3b Metastasis in internal mammary and axillary lymph nodes
- cN3c Metastasis in supraclavicular lymph node(s)

Notes

* Clinically detected is defined as detected by clinical examination or by imaging studies (excluding lymphoscintigraphy) and having characteristics highly suspicious for malignancy or a presumed pathological macrometastasis based on fine-needle aspiration biopsy with cytological examination. Confirmation of clinically detected metastatic disease by fine needle aspiration without excision biopsy is designated with a (f) suffix, e.g., cN3a(f).

Excisional biopsy of a lymph node or biopsy of a sentinel node, in the absence of assignment of a pT, is classified as a clinical N, e.g., cN1. Pathological classification (pN) is used for excision or sentinel lymph node biopsy only in conjunction with a pathological T assignment.

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

pT – Primary Tumour

The pathological classification requires the examination of the primary carcinoma with no gross tumour at the margins of resection. A case can be classified pT if there is only microscopic tumour in a margin.

The pT categories correspond to the cT categories.

Note

When classifying pT, the tumour size is a measurement of the invasive component. If there is a large in situ component (e.g., 4 cm) and a small invasive component (e.g., 0.5 cm), the tumour is coded pT1a.

pN – Regional Lymph Nodes

The pathological classification requires the resection and examination of at least the low axillary lymph nodes (level I) (see page 151). Such a resection will ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

pNX Regional lymph nodes cannot be assessed (e.g., previously removed or not removed for pathological study)
pN0 No regional lymph node metastasis*

Note

* Isolated tumour cell clusters (ITC) are single tumour cells or small clusters of cells not more than 0.2 mm in greatest extent that can be detected by routine H and E stains or immunohistochemistry. An additional criterion has been proposed to include a cluster of fewer than 200 cells in a single histological cross-section. Nodes containing only ITCs are excluded from the total positive node count for purposes of N classification and should be included in the total number of nodes evaluated (see Introduction, page 7).

pN1 Micrometastases or metastases in 1–3 axillary ipsilateral lymph nodes and/or in internal mammary nodes with metastases detected by sentinel lymph node biopsy but not clinically detected*
  pN1mi Micrometastases (larger than 0.2 mm and/or more than 200 cells, but not larger than 2.0 mm)

pN1a Metastasis in 1–3 axillary lymph node(s), including at least one larger than 2 mm in greatest dimension

pN1b Internal mammary lymph nodes not clinically detected

pN1c Metastasis in 1–3 axillary lymph nodes and internal mammary lymph nodes not clinically detected.

pN2 Metastasis in 4–9 ipsilateral axillary lymph nodes or in clinically detected* ipsilateral internal mammary lymph node(s) in the absence of axillary lymph node metastasis

pN2a Metastasis in 4–9 axillary lymph nodes, including at least one that is larger than 2 mm

pN2b Metastasis in clinically detected internal mammary lymph node(s), in the *absence* of axillary lymph node metastasis

pN3

pN3a Metastasis in 10 or more ipsilateral axillary lymph nodes (at least one larger than 2 mm) or metastasis in infraclavicular lymph nodes/level III lymph nodes

pN3b Metastasis in clinically detected* internal ipsilateral mammary lymph node(s) in the *presence* of positive axillary lymph node(s) or metastasis in more than three axillary lymph nodes *and* in internal mammary lymph nodes with microscopic or macroscopic metastasis detected by sentinel lymph node biopsy but not clinically detected

pN3c Metastasis in ipsilateral supraclavicular lymph node(s)

Post-treatment yp Classification:

- Post-treatment y-pathological (yp) classification should be based on the y-clinical stage information supplemented and/or modified by operative findings and pathological evaluation of the resection specimen.
- ypT and ypN categories correspond to the pT and pN categories, respectively. The ypT category must be based on the largest continuous focus of residual invasive cancer (if present and not including treatment-related fibrosis). Multiple foci of residual cancer should be classified accordingly with the 'm' suffix. The inclusion of additional information in the pathology report to estimate the extent of residual disease by the 'residual cancer burden method' is recommended.[1]
- The modifier 'sn' is used only if a sentinel node evaluation was performed after treatment. If no subscript is attached, it is assumed that the axillary nodal evaluation was by axillary node dissection.
- The X classification should be used (ypNX) if no yp post-treatment SN or axillary dissection was performed.

Notes

* *Clinically detected* is defined as detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination and having characteristics highly suspicious for malignancy or a presumed pathological macrometastasis based on fine-needle aspiration biopsy with cytological examination.

Not clinically detected is defined as not detected by imaging studies (excluding lymphoscintigraphy) or by clinical examination.

pM – Distant Metastasis

For pM, see page 8.

G Histopathological Grading

For histopathological grading of invasive carcinoma, the Nottingham Histological Score is recommended.[2]

Stage[a]

Stage 0	Tis	N0	M0
Stage IA	T1[b]	N0	M0
Stage IB	T0, T1	N1mi	M0
Stage IIA	T0, T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0, T1, T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	T4	N0, N1, N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Notes

[a] The AJCC also publish a prognostic group for breast tumours.

[b] T1 includes T1mi.

Prognostic Factors Grid – Breast

Prognostic factors for breast cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Inflammatory breast cancer Histological grade ER, HER2 receptor Number and percentage of involved nodes Tumour size Presence of lymphatic or vascular invasion (LVI+) Surgical resection margin status	Age Menopausal status Sex	Distance from treatment centre Access to specific investigations and/or treatments Experience of treating centre Socioeconomic status Prior radiation involving the chest or mediastinum (e.g. for Hodgkin disease)
Additional	Progesterone receptor Tumour profiling UPA, PAI-1 Ki-67 Gene-expression signatures Tumour-infiltrating lymphocytes (TILs) PD-L1 status in triple-negative breast	*BRCA1* or 2 mutation Obesity	Expertise of a treatment at the specific level (e.g., surgery or ablative therapies) Access to information Resection margin Use of postmenopausal hormone replacement therapy

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang.

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2 Elston CW, Ellis IO. Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer: experience from a large study with long-term follow-up. *Histopathology* 1991; 19: 403–410.

Gynaecological Tumours

Introductory Notes

The following sites are included:

- Vulva
- Vagina
- Cervix uteri
- Corpus uteri
  - Endometrium
  - Uterine sarcomas
- Ovary, Fallopian tube and primary peritoneal carcinoma
- Gestational trophoblastic tumours

Cervix uteri and corpus uteri were among the first sites to be classified by the TNM system. Originally, carcinoma of the cervix uteri was staged following the rules suggested by the Radiological Sub-Commission of the Cancer Commission of the Health Organization of The League of Nations. These rules were then adopted, with minor modifications, by the newly formed Fédération Internationale de Gynécologie et d'Obstétrique (FIGO). Finally, UICC brought them into the TNM in order to correspond to the FIGO stages. FIGO, UICC and AJCC work in close collaboration in the revision process.

Histopathological Grading

The definitions of the G categories apply to all carcinomas. These are:

G – Histopathological Grading

GX Grade of differentiation cannot be assessed
G1 Well-differentiated
G2 Moderately differentiated
G3 Poorly differentiated or undifferentiated

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Vulva
(ICD-O-4 C51)

The definitions of the T, N and M categories correspond to the FIGO stages[1] and AJCC 9th version. The FIGO system is included for comparison.

Rules for Classification

The classification applies only to primary carcinomas and germ cell tumours of the vulva. There should be histological confirmation of the disease.

Regional Lymph Nodes

The regional lymph nodes are the femoral and inguinal (groin) nodes.

TNM Clinical Classification

T – Primary tumour

	FIGO stage	
cTX	N/A	Primary tumour cannot be assessed
cT0	N/A	No evidence of primary tumour
cTis	N/A	Carcinoma in situ (preinvasive carcinoma), high grade HPV-associated squamous intraepithelial lesion (VIN II or III), HPV-independent vulvar intraepithelial neoplasia (differentiated VIN)
cT1	I	Tumour confined to vulva or vulva and perineum
cT1a	IA	Tumour 2 cm or less in greatest dimension and with stromal invasion not greater than 1.0 mm*
cT1b	IB	Tumour greater than 2 cm and/or with stromal invasion greater than 1 mm*
cT2	II	Tumour of any size invades lower third urethra, lower third vagina or anus
cT3	III	Tumour of any size invades upper two-thirds urethra, upper two-thirds vagina, bladder mucosa or rectal mucosa
cT4	IVA	Tumour fixed to pelvic bone

Note

* Depth of invasion is now measured from the basement membrane of the deepest adjacent dysplastic tumour-free rete ridge to the deepest point of invasion (this is a change from method of measurement from TNM8).

N – Regional Lymph Nodes

	FIGO stage	
cNX	N/A	Regional lymph nodes cannot be assessed
cN0	N/A	No regional lymph node metastasis
N0(i+)	N/A	Isolated tumour cells in regional lymph node(s) ≤0.2 mm, or single cells or clusters of cells ≤200 cells in a single lymph node cross-section
cN1	III	Tumour involvement of non-fixed, non-ulcerated regional lymph nodes
cN1mi	IIIA	Tumour involvement (>0.2 mm but ≤2.0 mm in diameter) of regional lymph nodes
cN1a	IIIA	Tumour involvement (>2.0 mm to but ≤5 mm) of regional lymph nodes
cN1b	IIIB	Tumour involvement (>5 mm) of regional lymph nodes N1c; tumour involvement of regional lymph nodes with extranodal extension (ENE)
cN2	IVA	Tumour involvement of fixed or ulcerated regional lymph nodes

M – Distant Metastasis

	FIGO stage	
cM0	N/A	No distant metastasis
cM1	IVB	Distant metastasis (including pelvic lymph node metastasis)

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

pN0 Histological examination of an inguinofemoral lymphadenectomy specimen should ordinarily include six or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0

Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
	TX-T3	N1a, N1mi	M0
Stage IIIB	TX-T3	N1b	M0
Stage IIIC	TX-T3	N1c	M0
Stage IVA	T4	Any N	M0
	Any T	N2	M0
Stage IVB	Any T	Any N	M1

Prognostic Factors Grid – Vulva

Prognostic risk factors for cancer of the vulva

Prognostic factors	Tumour related	Host related	Environment related
Essential	TNM Number Lymph node metastases Lymphovascular invasion Perineural invasion Resection margin	Age Smoking Immune status	Distance from treatment centre Access to specific investigations and/or treatments Experience of treating centre Socioeconomic status
Additional	Diameter of primary tumour Histological type Multifocal disease P16/HPV status P53 overexpression	Adjacent dermatosis (Lichen sclerosus, vulva intraepithelial neoplasia)	Expertise of a treatment at the specific level (e.g., surgery or ablative therapies) Access to information Resection margin

Vagina
(ICD-O-4 C52)

The definitions of the T and M categories correspond to the FIGO stages and AJCC 8th edition/version. The FIGO system is included for comparison.

Rules for Classification

The classification applies to primary carcinomas only. Tumours present in the vagina as secondary growths from either genital or extragenital sites are excluded. A tumour that has extended to the portio and reached the external os (orifice of uterus) is classified as carcinoma of the cervix. A vaginal carcinoma occurring 5 years after successful treatment (complete response) of a carcinoma of the cervix uteri is considered a primary vaginal carcinoma. A tumour involving the vulva is classified as carcinoma of the vulva. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N and M categories:

T categories	Physical examination, endoscopy and imaging
N categories	Physical examination and imaging
M categories	Physical examination and imaging

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

Regional Lymph Nodes

Upper two-thirds of vagina	the pelvic nodes including obturator, internal iliac (hypogastric), external iliac and pelvic nodes, NOS.
Lower third of vagina	the inguinal and femoral nodes.

TNM Clinical Classification

T – Primary Tumour

cTNM Categories	FIGO Stage	Definition
cTX		Primary tumour cannot be assessed
cT0		No evidence of primary tumour
cTis		Carcinoma in situ (preinvasive carcinoma); high grade squamous intraepithelial lesion
cT1	I	Tumour confined to vagina

(*Continued*)

(Continued)

cTNM Categories	FIGO Stage	Definition
cT2	II	Tumour invades paravaginal tissues (paracolpium)
cT3	III	Tumour extends to the pelvic wall
cT4	IVA	Tumour invades *mucosa* of bladder or rectum or extends beyond the true pelvis*
cM1	IVB	Distant metastasis

Note

* The presence of bullous oedema is not sufficient evidence to classify a tumour as T4.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

TNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of an inguinal lymphadenectomy specimen should ordinarily include six or more lymph nodes; a pelvic lymphadenectomy specimen should ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Cervix Uteri
(ICD-O-4 C53)

The definitions of the T, N and M categories correspond to the FIGO stages[1] and AJCC 9th version. The FIGO system is included for comparison.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

Note
Imaging and pathology can be used, when available, to supplement clinical findings with respect to tumour size and extent, in all stages.

Anatomical Subsites

1. Endocervix (C53.0)
2. Exocervix (C53.1)

Regional Lymph Nodes

The regional lymph nodes are the paracervical, parametrial, hypogastric (internal iliac, obturator), common and external iliac, presacral, lateral sacral nodes and paraaortic nodes.

TNM Clinical Classification

cT – Primary Tumour

TNM Categories	FIGO Stage	
cTX		Primary tumour cannot be assessed
cT0		No evidence of primary tumour
cTis		Carcinoma in situ (preinvasive carcinoma)*
cT1	I	Tumour confined to the cervix (extension to corpus should be disregarded)
cT1a	IA	Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximal depth of 5.0 mm**

(Continued)

(Continued)

TNM Categories	FIGO Stage	
cT1a1	IA1	Measured depth of stromal invasion 3.0 mm or less in depth**
cT1a2	IA2	Measured depth of stromal invasion more than 3.0 mm** and not more than 5.0 mm
cT1b	IB	Lesion confined to the cervix with depth of invasion greater than 5 mm**
cT1b1	IB1	Lesion 2.0 cm or less in greatest dimension
cT1b2	IB2	Lesion more than 2.0 cm in greatest dimension but not more than 4 cm in greatest dimension.
cT1b3	IB3	Lesion more than 4 cm in greatest diameter
cT2	II	Tumour invades beyond uterus but not to the pelvic wall or to the lower third of vagina
cT2a	IIA	Tumour without parametrial invasion
cT2a1	IIA1	Lesion 4.0 cm or less in greatest dimension
cT2a2	IIA2	Lesion more than 4.0 cm in greatest dimension
cT2b	IIB	Tumour with parametrial invasion
cT3	III	Tumour involves lower third of vagina or extends to pelvic wall or causes hydronephrosis or non-functioning kidney
cT3a	IIIA	Tumour involves lower third of vagina
cT3b	IIIB	Tumour extends to pelvic wall or causes hydronephrosis or non-functioning kidney
cT4	IVA	Tumour invades mucosa of the bladder or rectum or extends beyond true pelvis***

Notes

* No FIGO equivalent; FIGO does not include Stage 0 (Tis).

** The depth of invasion should be taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defined as the measurement of the tumour from the epithelial–stromal junction of the adjacent most superficial papillae to the deepest point of invasion.

*** Bullous oedema is not sufficient to classify a tumour as T4.

N – Regional lymph nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis to pelvic lymph nodes only
cN2 Regional lymph node metastasis to para-aortic lymph nodes, with or without positive pelvic lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis (includes inguinal lymph nodes and intraperitoneal disease). It excludes metastasis to vagina, pelvic serosa but does include uterine serosa, and adnexa[1]

Note

[1] FIGO excludes uterine serosa and adnexal involvement from M1. UICC and AJCC align and include uterine serosa and adnexal involvement in M1.

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a pelvic lymphadenectomy specimen should ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IA1	T1a1	N0	M0
Stage IA2	T1a2	N0	M0
Stage IB	T1b	N0	M0
Stage IB1	T1b1	N0	M0
Stage IB2	T1b2	N0	M0
Stage II	T2	N0	M0
Stage IIA	T2a	N0	M0
Stage IIA1	T2a1	N0	M0
Stage IIA2	T2a2	N0	M0
Stage IIB	T2b	N0	M0
Stage III	T3	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	Any N	M0
	T1, T2, T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Prognostic Factors Grid – Cervix Uteri

Prognostic risk factors in cervical cancer

Prognostic factors	Tumour related	Host related	Environment *related
Essential	TNM Unilateral vs bilateral disease Positive surgical margins	Immunosuppression (i.e. HIV infection) Performance status Morbid obesity Smoking history	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Lymphovascular space invasion Histological type P16/HPV status PDL-1 status	Anaemia during treatment	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Bhatla N, Berek JS, Cuello Fredes M, et al., Revised FIGO staging for carcinoma of the cervix uteri. Int J Gynecol Obstet 2019; 145: 129–135. doi:https://doi.org/10.1002/ijgo.12749. Also the corrigendum. Int J Gynecol Obstet; 147: 279–280. doi:10.1002/ijgo.12969; Int J Gynecol Obstet. 2021; 155: 43–47. doi:10.1002/ijgo.13880.

Uterus – Endometrium
(ICD-O-4 C54.0-1, C54.3, C54.8, C54.9, C55)

The definitions of the T, N and M categories correspond to the AJCC 8th edition/ version.

Rules for Classification

The classification applies to endometrial carcinomas and carcinosarcomas. There should be histological verification with subdivision by histological type and grading of the carcinomas.

1. Isthmus uteri (C54.0)
2. Fundus uteri (C54.3)
3. Endometrium (C54.1)

Regional Lymph Nodes

The regional lymph nodes are the pelvic (hypogastric [obturator, internal iliac], common and external iliac, parametrial and sacral) and the para-aortic nodes.

TNM Clinical Classification

T – Primary Tumour

TNM Categories

cTX	Primary tumour cannot be assessed	
cT0	No evidence of primary tumour	
cT1	Tumour confined to the corpus uteri*	
	cT1a	Tumour limited to endometrium or invading less than half of myometrium
	cT1b	Tumour invades one half or more of myometrium
cT2	Tumour invades cervical stroma but does not extend beyond the uterus	
cT3**	Local and/or regional spread as specified here:	
	cT3a	Tumour invades the serosa of the corpus uteri or adnexae (direct extension or metastasis)
	cT3b	Vaginal or parametrial involvement (direct extension or metastasis)
cT4***	Tumour invades bladder/bowel mucosa	

Notes

* Endocervical glandular involvement only should be considered as stage I.

** Positive cytology has to be reported separately without changing the stage.

*** The presence of bullous oedema is not sufficient evidence to classify the case as T4.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis to pelvic lymph nodes
cN2 Regional lymph node metastasis to para-aortic lymph nodes with or without metastasis to pelvic lymph nodes

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis (excluding metastasis to vagina, pelvic serosa or adnexa, including metastasis to inguinal lymph nodes, intra-abdominal lymph nodes other than para-aortic or pelvic nodes)

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a pelvic lymphadenectomy specimen should ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

G Histopathological Grading

For histopathological grading, use G1, G2 or G3. For details, see Creasman et al.[1]

Stage

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC1	T1, T2, T3	N1	M0
Stage IIIC2	T1, T2, T3	N2	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Prognostic Grid – Endometrium

Prognostic factors for endometrial carcinoma and carcinosarcoma

Prognostic factors	Tumour related	Host related	Environment related
Essential	TNM Depth of myometrial invasion Grade of differentiation Tumour cell type Lymphovascular space invasion	Obesity	Postsurgical treatment
Additional	Metastasis to lymph nodes Site of distant metastasis Molecular profile (POLE, Mismatch repair and P53 status)	Age Performance status Race Co-morbidities	Extent of resection Postsurgical treatment

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Creasman WT, Odicino F, Maisoneuve P, et al. FIGO Annual Report on the results of treatment in gynaecological cancer. Vol. 26. Carcinoma of the corpus uteri. *Int J Gynecol Obstet* 2006; 95 (Suppl. 1): 105–143.

Uterine Sarcomas
(Leiomyosarcoma, Endometrial Stromal Sarcoma, Adenosarcoma) (ICD-O-4 C53, C54, 55)

The definitions of the T, N and M categories correspond to the FIGO stages and AJCC 8th edition/version. FIGO system is included for comparison.[1,2]

Rules for Classification

The classification applies to sarcomas not including carcinosarcoma, which is classified as carcinoma of the endometrium. There should be histological confirmation and division of cases by histological type.

The following are the procedures for assessing T, N and M categories:

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

Anatomical Subsites

1. Cervix uteri (C53)
2. Isthmus uteri (C54.0)
3. Myometrium (C54.2)
4. Fundus uteri (C54.3)

Regional Lymph Nodes

The regional lymph nodes are the pelvic (hypogastric [obturator, internal iliac], common and external iliac, parametrial and sacral) and the para-aortic nodes.

TNM Clinical Classification

Leiomyosarcoma, Endometrial stromal sarcoma

T – Primary Tumour

TNM categories	FIGO stage	Definition
cT1	I	Tumour limited to the uterus
cT1a	IA	Tumour 5 cm or less in greatest dimension
cT1b	IB	Tumour more than 5 cm
cT2	II	Tumour extends beyond the uterus, within the pelvis
cT2a	IIA	Tumour involves adnexa
cT2b	IIB	Tumour involves other pelvic tissues

(Continued)

TNM categories	FIGO stage	Definition
cT3	III	Tumour infiltrates abdominal tissues
cT3a	IIIA	One site
cT3b	IIIB	More than one site
cN1	IIIC	Metastasis to regional lymph nodes
cT4	IVA	Tumour invades bladder or rectum
cM1	IVB	Distant metastasis

Note

Simultaneous tumours of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumours.

Adenosarcoma

T – Primary Tumour

TNM categories	FIGO stage	Definition
cT1	I	Tumour limited to the uterus
cT1a	IA	Tumour limited to the endometrium/endocervix
cT1b	IB	Tumour invades to less than half of the myometrium
cT1c	IC	Tumour invades more than half of the myometrium
cT2	II	Tumour extends beyond the uterus, within the pelvis
cT2a	IIA	Tumour involves adnexa
cT2b	IIB	Tumour involves other pelvic tissues
cT3	III	Tumour involves abdominal tissues
cT3a	IIIA	One site
cT3b	IIIB	More than one site
cN1	IIIC	Metastasis to regional lymph nodes
cT4	IVA	Tumour invades bladder or rectum
cM1	IVB	Distant metastasis

Note

Simultaneous tumours of the uterine corpus and ovary/pelvis in association with ovarian/pelvic endometriosis should be classified as independent primary tumours.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage – Uterine Sarcomas

Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IC*	T1c	N0	M0
Stage II	T2	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T1, T2, T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

Note

* Stage IC does not apply for leiomyosarcoma and endometrial stromal sarcoma.

References

1 Prat J. FIGO staging for uterine sarcomas. *Int J Gynaecol Obstet* 2009; 104: 177–178.
2 FIGO Committee on Gynecologic Oncology Report. FIGO staging for uterine sarcomas. *Int J Gynaecol Obstet* 2009; 104: 179.

Ovarian, Fallopian Tube and Primary Peritoneal Carcinoma

(ICD-O-4 C48.1-2, C56, C57)

The definitions of the T, N and M categories correspond to the FIGO stages and AJCC 8th edition/version. FIGO system is included for comparison.

Rules for Classification

The classification applies to malignant ovarian neoplasms of both epithelial and stromal origin including borderline tumours[1] corresponding to 'common epithelial tumours' of the earlier terminology.

The classification also applies to malignant and borderline epithelial and stromal tumours of the Fallopian tube and peritoneum (Müllerian origin).

There should be histological confirmation of the disease and division of cases by histological type.

The following are the procedures for assessing T, N and M categories:

T categories	Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)
N categories	Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)
M categories	Clinical examination, imaging, surgical exploration (laparoscopy/laparotomy)

The FIGO stages are based on surgical staging. (TNM stages are based on clinical and/or pathological classification.)

Regional Lymph Nodes

The regional lymph nodes are the hypogastric (obturator), common iliac, external iliac, lateral sacral, para-aortic and retroperitoneal nodes.*

Note

* Including intra-abdominal node such as greater omental nodes.

TNM Clinical Classification

T – Primary Tumour

TNM categories	FIGO stage	Definition
cTX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
T1	I	Tumour limited to the ovaries (one or both) or Fallopian tube(s)
T1a	IA	Tumour limited to one ovary (capsule intact) or Fallopian tube; capsule intact, no tumour on ovarian surface or Fallopian tube surface; no malignant cells in ascites or peritoneal washings
T1b	IB	Tumour limited to both ovaries or Fallopian tubes; capsule intact, no tumour on ovarian or Fallopian tube surface; no malignant cells in ascites or peritoneal washings
T1c	IC	Tumour limited to one or both ovaries or Fallopian tubes with any of the following:
cT1c1	IC1	Surgical spill
cT1c2	IC2	Capsule ruptured before surgery or tumour on ovarian or Fallopian tube surface
cT1c3	IC3	Malignant cells in ascites or peritoneal washings
cT2	II	Tumour involves one or both ovaries or Fallopian tubes with pelvic extension (below the pelvic brim) or primary peritoneal cancer
cT2a	IIA	Extension and/or implants on uterus and/or Fallopian tube(s) and or ovary(ies)
cT2b	IIB	Extension to other pelvic tissues, including bowel within the pelvis
cT3 and/or cN1	III[a]	Tumour involves one or both ovaries or Fallopian tubes or primary peritoneal carcinoma with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes

(*Continued*)

TNM categories	FIGO stage	Definition
cN1		Retroperitoneal lymph node metastasis only
cN1a	IIIA1i	Lymph node metastasis not more than 10 mm in greatest dimension
cN1b	IIIA1ii	Lymph node metastasis more than 10 mm in greatest dimension
cT3a any N	IIIA2	Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without retroperitoneal lymph node, including bowel involvement
cT3b any N	IIIB	Macroscopic peritoneal metastasis beyond pelvic brim 2 cm or less in greatest dimension, including bowel involvement outside the pelvis with or without retroperitoneal nodes
cT3c any N	IIIC	Peritoneal metastasis beyond pelvic brim more than 2 cm in greatest dimension and/or retroperitoneal lymph node metastasis (includes extension of tumour to capsule of liver and spleen without parenchymal involvement of either organ)
cM1	IV	Distant metastasis (excludes peritoneal metastasis)
cM1a	IVA	Pleural effusion with positive cytology
cM1b[b]	IVB	Parenchymal metastasis and metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity)

Notes

[a] Liver capsule metastasis is T3/stage III.

[b] Liver parenchymal metastasis M1/stage IV.

N – Regional Lymph Nodes

TNM categories	FIGO stage	Definition
cNX		Regional lymph nodes cannot be assessed
cN0		No regional lymph node metastasis
cN1		Regional lymph node metastasis
cN1	IIIA1	Retroperitoneal lymph node metastasis only
cN1a	IIIA1i	Lymph node metastasis not more than 10 mm in greatest dimension
cN1b	IIIA1ii	Lymph node metastasis more than 10 mm in greatest dimension

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
cM1a Pleural effusion with positive cytology
cM1b Parenchymal metastasis and metastasis to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside the abdominal cavity)

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

pN0 Histological examination of a pelvic lymphadenectomy specimen should ordinarily include 10 or more lymph nodes. If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0.

Stage

Stage I	T1	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IC	T1c	N0	M0
Stage II	T2	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIIA1	T1/2	N1	M0
Stage IIIA2	T3a	N0, N1	M0
Stage IIIB	T3b	N0, N1	M0
Stage IIIC	T3c	N0, N1	M0
Stage IV	Any T	Any N	M1
Stage IVA	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Prognostic Factors Grid – Tumours of the Ovary, Fallopian Tube and Peritoneal Carcinoma

Prognostic risk factor for epithelial ovarian cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Histological type Grade TNM Residual disease	Age Co-morbidities Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Nodal involvement Site of metastasis DNA ploidy CA125 BRCA1/2 HR status, microsatellite instability (MSI), mismatch repair (MMR), tumour mutational burden (TMB), BRAF and NTRK.	*BRCA 1* Genetic predisposition	Expertise of a treatment at the specific level (e.g., surgery or radiotherapy) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Reference

1 Prat J, FIGO Committee on Gynecologic Oncology. Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynecol Obstet* 2014; 124: 1–5.

Gestational Trophoblastic Neoplasms
(ICD-O-4 C58)

The following classification for gestational trophoblastic tumours is based on that of FIGO adopted in 1992 and updated in 2002.[1] The definitions of T and M categories correspond to the FIGO stages and AJCC 8th edition/version. FIGO system is included for comparison. In contrast to other sites, an N (regional lymph node) classification does not apply to these tumours. A prognostic scoring index, which is based on factors other than the anatomical extent of the disease, is used to assign cases to high-risk and low-risk categories, and these categories are used in stage grouping.

Rules for Classification

The classification applies to choriocarcinoma, invasive hydatidiform mole, epithelioid trophoblastic tumour and placental site trophoblastic tumour. Placental site tumours should be reported separately. Histological confirmation is not required if the human chorionic gonadotropin (βhCG) level is abnormally elevated. History of prior chemotherapy for this disease should be noted.

The following are the procedures for assessing T and M categories:

T categories Clinical examination, imaging and endoscopy, and serum/urine βhCG level

M categories Clinical examination, imaging and assessment of serum/urine βhCG level

Risk categories Age, type of antecedent pregnancy, interval months from index pregnancy, pre-treatment **serum/urine** βhCG, diameter of largest tumour, site of metastasis, number of metastases and previous failed chemotherapy are integrated to provide a prognostic score that divides cases into low- and high-risk categories.

TM Clinical Classification

T – Primary Tumour

TM categories	FIGO stages[a]	Definition
cTX		Primary tumour cannot be assessed
cT0		No evidence of primary tumour
cT1	I	Tumour confined to uterus
cT2[b]	II	Tumour extends to other genital structures: vagina, ovary, broad ligament orFallopian tube by metastasis or direct extension

(Continued)

TM categories	FIGO stages[a]	Definition
cM1a	III	Metastasis to lung(s)
cM1b[c]	IV	Other distant metastasis

Notes

[a] Stages I to IV are subdivided into A and B according to the prognostic score.

[b] Genital metastasis (vagina, ovary, broad ligament, Fallopian tube) is classified as T2.

[c] Any involvement of non-genital structures, whether by direct invasion or metastasis is described using the M classification.

pTM Pathological Classification

The pT categories correspond to the cT categories. For pM, see page 8.

Stage

Stage I	T1	M0
Stage II	T2	M0
Stage III	Any T	M1a
Stage IV	Any T	M1b

Prognostic Score

Prognostic factor	0	1	2	4
Age	<40	≥40		
Antecedent pregnancy	H. mole	Abortion	Term pregnancy	
Months from index pregnancy	<4	4–6	7–12	>12
Pre-treatment serum hCG (IU/ml)	$<10^3$	10^3– $<10^4$	10^4– $<10^5$	$\geq 10^5$
Largest tumour size including uterus	<3 cm	3–5 cm	>5 cm	

(Continued)

(Continued)

Prognostic factor	0	1	2	4
Sites of metastasis	Lung	Spleen, kidney	Gastrointestinal tract	Liver, brain
Number of metastasis		1–4	5– 8	>8
Previous failed chemotherapy			Single drug	Two or more drugs

Risk categories:
Total prognostic score 6 or less = low risk
Total score 7 or more = high risk

Prognostic Group

Record stage and prognostic score separated by a colon, i.e., **II: 4 or IV: 9**.

Reference

1 Ngan HYS, Bender H, Benedet JL, Jones H, Montrucolli GC, Pecorelli S; FIGO Committee on Gynecologic Oncology. Gestational trophoblastic neoplasia. *Int J Gynecol Obstet* 2002; 77: 285–287.

Urological Tumours

Introductory Notes

The following sites are included:

- Penis
- Prostate
- Testis
- Kidney
- Renal pelvis and ureter
- Urinary bladder
- Urethra

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Penis
(ICD-O-4 C60)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to carcinomas. There should be histological confirmation of the disease.

Anatomical Subsites

1. Prepuce (C60.0)
2. Glans penis (C60.1)
3. Body of penis (C60.2)

Regional Lymph Nodes

The regional lymph nodes are the superficial and deep inguinal and the pelvic nodes.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ (Penile intraepithelial neoplasia – PeIN)
cTa Non-invasive localised squamous cell carcinoma[1]

cT1 Tumour invades subepithelial connective tissue[2]
- cT1a Tumour invades subepithelial connective tissue without lymphovascular invasion or perineural invasion and is not poorly differentiated
- cT1b Tumour invades subepithelial connective tissue with lymphovascular invasion or perineural invasion or is poorly differentiated

cT2 Tumour invades corpus spongiosum with or without invasion of the urethra
cT3 Tumour invades corpus cavernosum with or without invasion of the urethra
cT4 Tumour invades other adjacent structures

Notes

[1] Including verrucous carcinoma.

[2] Glans: Tumour invades lamina propria
Foreskin: Tumour invades dermis, lamina propria or dartos fascia
Shaft: Tumour invades connective tissue between epidermis and corpora and regardless of location.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No palpable or visibly enlarged inguinal lymph nodes
cN1 Palpable mobile unilateral inguinal lymph node
cN2 Palpable mobile multiple or bilateral inguinal lymph nodes
cN3 Fixed inguinal nodal mass or pelvic lymphadenopathy unilateral or bilateral

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the cT categories. The pN categories are based on biopsy or surgical excision. For pM, see page 8.

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis in one or two inguinal lymph nodes
pN2 Metastasis in more than two unilateral inguinal nodes or bilateral inguinal lymph nodes
pN3 Metastasis in pelvic lymph node(s), unilateral or bilateral or extranodal extension of regional lymph node metastasis

Stage

Stage 0	Tis	N0	M0
	Ta	N0	M0
Stage I	T1a	N0	M0
Stage IIA	T1b,T2	N0	M0
Stage IIB	T3	N0	M0
Stage IIIA	T1, T2, T3	N1	M0
Stage IIIB	T1, T2, T3	N2	M0
Stage IV	T4	Any N	M0
	Any T	N3	M0
	Any T	Any N	M1

Prognostic Factors Grid – Penis

Prognostic factors for survival for squamous cell carcinoma

Prognostic factor	Tumour related	Host related	Environment related*
Essential	TNM Grade Lymphovascular space invasion	History of genital condylomas Lichen sclerosus Poor hygiene	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	HPV/p16	Smoking HIV/immune suppression	Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang.

Prostate
(ICD-O-4 C61.9)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to carcinomas excluding urothelial carcinoma of the prostate, which is classified as a urethral tumour (see page 201). There should be histological confirmation of the disease.

Regional Lymph Nodes

The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. Laterality does not affect the N classification.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Clinically inapparent tumour that is not palpable
- cT1a Tumour incidental histological finding in 5% or less of tissue resected
- cT1b Tumour incidental histological finding in more than 5% of tissue resected
- cT1c Tumour identified by needle biopsy (e.g., because of elevated PSA)

cT2 Tumour that is palpable and confined within prostate
- cT2a Tumour involves one half of one lobe or less
- cT2b Tumour involves more than half of one lobe, but not both lobes
- cT2c Tumour involves both lobes

cT3 Tumour extends through the prostatic capsule*
- cT3a Extraprostatic extension (unilateral or bilateral) including microscopic bladder neck involvement
- cT3b Tumour invades seminal vesicle(s)

cT4 Tumour is fixed or invades adjacent structures other than seminal vesicles: external sphincter, rectum, levator muscles and/or pelvic wall

Note

* Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is not classified as cT3, but as cT2.

N – Regional Lymph Nodes[1]

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis[2]

M0 No distant metastasis
M1 Distant metastasis
- M1a Non-regional lymph node(s)
- M1b Bone(s)
- M1c Other site(s)

Notes

Due to the effect of stage migration (see page 14), it is important that the procedures for determining the T, N, and M categories are recorded when known. The use of different imaging techniques in prostate cancer has resulted in increasing stage migration, particularly when MRI is used rather than palpation to determine the T category or PSMAPET is used to assess lymph node status and metastases. If the imaging technique used is known, the suffix abbreviations for MRI and PET below should be used. If not known or nor recorded, it is assumed that the T category has been determined by palpation
MRI: (mr), e.g., T2b(mr), Stage II(mr)
PSMAPET: (PET), e.g., N1(PET), Stage IV(PET)

[1] Metastasis *no larger* than 0.2 cm can be designated pNmi. (See Introduction, pN, page 7.)
[2] When more than one site of metastasis is present, the most advanced category is used. (p)M1c is the most advanced category.

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.
However, there is no pT1 category because there is insufficient tissue to assess the highest pT category. There are no sub-categories of pT2.

G Histopathological Grade Group

GX Grade cannot be assessed

Grade group	Gleason score	Gleason pattern
1	≤6	≤3 + 3
2	7	3 + 4
3	7	4 + 3
4	8	4 + 4, 5 + 3, 3 + 5
5	9–10	4 + 5, 5 + 4, 5 + 5

Clinical Stage

Stage I	T1, cT2a	N0	cM0
Stage II	pT2	cN0	cM0
	cT2b, cT2c	N0	cM0
Stage III	T3, T4	N0	cM0
Stage IV	Any T	N1	cM0
	Any T	Any N	cM1

Pathological Stage[1,2]

Stage II	pT2	pN0	cM0
Stage III	pT3, pT4	pN0	cM0
Stage IV	Any pT	pN1	cM0
	Any T	Any N	pM1

Notes

[1] There is no pathological Stage I.

[2] The AJCC also publish a prognostic group for prostate tumours.

Prognostic Factors Grid – Prostate

Prognostic factors for prostate cancer

Prognostic factor	Tumour related	Host related	Environment related*
Essential	Gleason score Grade group TNM PSA level % involvement of cores on biopsy and number of positive cores	Co-morbidity Age Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Intraductal and/or cribriform histologies PSA density Alkaline phosphatase (if bone metastases) Gene expression assays Somatic DNA repair gene alterations	Germline DNA repair gene alterations (e.g. BRCA1/2, ATM, PALB2, CHEK2, etc.) Lynch syndrome	Expertise of a treatment at the specific level (surgery or radiotherapy and brachytherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Testis
(ICD-O-4 C62)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to germ cell tumours of the testis. There should be histological confirmation of the disease and division of cases by histological type. Histopathological grading is not applicable.

The presence of elevated serum tumour markers, including alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG) and lactate dehydrogenase (LDH), is frequent in this disease. Staging is based on the determination of the anatomical extent of disease and assessment of serum tumour markers.

Stages are subdivided based on the presence and degree of elevation of serum tumour markers. Serum tumour markers are obtained immediately after orchiectomy and, if elevated, should be performed serially after orchiectomy according to the normal decay for AFP (half-life 7 days) and hCG (half-life 3 days) to assess for serum tumour marker elevation. The S classification is based on the nadir value of hCG and AFP after orchiectomy. The serum level of LDH (but not its half-life levels) has prognostic value in patients with metastatic disease and is included in staging.

Regional Lymph Nodes

The regional lymph nodes are the abdominal para-aortic (periaortic), preaortic, interaortocaval, precaval, paracaval, retrocaval and retroaortic nodes. Nodes along the spermatic vein should be considered regional. Laterality does not affect the N classification. The intrapelvic nodes and the inguinal nodes are considered regional after scrotal or inguinal surgery performed before the diagnosis of the testis tumour.

TNM Clinical Classification

T – Primary Tumour

Except for pTis and pT4, where radical orchiectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchiectomy; see pT. In other circumstances, TX is used if no radical orchiectomy has been performed.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, not more than 2 cm in greatest dimension
cN2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension, or multiple lymph nodes, any one mass more than 2 cm but not more than 5 cm in greatest dimension
cN3 Metastasis with a lymph node mass more than 5 cm in greatest dimension

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
M1a Non-regional lymph node(s) or lung metastasis
M1b Distant metastasis other than non-regional lymph nodes and lung

pTNM Pathological Classification

pT – Primary Tumour

pTX Primary tumour cannot be assessed (see T – Primary Tumour)
pT0 No evidence of primary tumour (e.g., histological scar in testis)
pTis Intratubular germ cell neoplasia (carcinoma in situ)

pT1 Tumour limited to testis, including the rete testis, but without vascular/lymphatic invasion or invasion of the epididymis; tumour may invade tunica albuginea but not tunica vaginalis[1]
pT2 Tumour limited to testis with vascular/lymphatic invasion, or invading hilar soft tissue or epididymis or tumour extending through tunica albuginea with involvement of tunica vaginalis
pT3 Tumour invades spermatic cord with or without vascular/lymphatic invasion[2]
pT4 Tumour invades scrotum with or without vascular/lymphatic invasion

Notes

[1] AJCC subdivides pT1 seminoma into pT1a and pT1b depending on size not greater than 3 cm or greater than 3 cm in greatest dimension.

[2] AJCC notes that discontinuous involvement of spermatic cord should be considered as M1.

pN – Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis

pN1 Metastasis with a lymph node mass 2 cm or less in greatest dimension and five or fewer positive nodes, not more than 2 cm in greatest dimension
pN2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than five nodes positive, not more than 5 cm; or evidence of extranodal extension of tumour
pN3 Metastasis with a lymph node mass more than 5 cm in greatest dimension

pM – Distant Metastasis

For pM, see page 8.

S – Serum Tumour Markers

SX Serum marker studies not available or not performed
S0 Serum marker study levels within normal limits

	LDH	hCG (mIU/ml)	AFP (ng/ml)
S1	<1.5 × N	and <5000	and <1000
S2	1.5–10 × N	or 5000–50 000	or 1000–10 000
S3	>10 × N	or >50 000	or >10 000

Note
N indicates the upper limit of normal for the LDH assay.

Prognostic Group

Stage 0	pTis	N0	M0	S0
Stage I	pT1–T4	N0	M0	SX
Stage IA	pT1	N0	M0	S0
Stage IB	pT2–T4	N0	M0	S0
Stage IS	Any pT/TX	N0	M0	S1–S3
Stage II	Any pT/TX	N1 – N3	M0	SX
Stage IIA	Any pT/TX	N1	M0	S0
	Any pT/TX	N1	M0	S1
Stage IIB	Any pT/TX	N2	M0	S0
	Any pT/TX	N2	M0	S1
Stage IIC	Any pT/TX	N3	M0	S0
	Any pT/TX	N3	M0	S1
Stage III	Any pT/TX	Any N	M1a	SX
Stage IIIA	Any pT/TX	Any N	M1a	S0
	Any pT/TX	Any N	M1a	S1
Stage IIIB	Any pT/TX	N1–N3	M0	S2
	Any pT/TX	Any N	M1a	S2
Stage IIIC	Any pT/TX	N1–N3	M0	S3

Any pT/TX	Any N	M1a	S3
Any pT/TX	Any N	M1b	Any S

Prognostic Factors Grid – Testis

Prognostic factors for testicular cancer

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Histological type TNM Tumour markers (nonseminoma) LDH (seminoma) Non pulmonary metastases	Age Performance Status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Rate of marker decline (nonseminoma)	Delay in diagnosis	Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Kidney
(ICD-O-4 C64)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to renal cell carcinomas. There should be histological confirmation of the disease. Nephroblastoma classification is in the paediatric chapter (see page 245).

Regional Lymph Nodes

The regional lymph nodes are the hilar, abdominal para-aortic and paracaval nodes. Laterality does not affect the N categories.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour 7 cm or less in greatest dimension, limited to the kidney
- cT1a Tumour 4 cm or less
- cT1b Tumour more than 4 cm but not more than 7 cm

cT2 Tumour more than 7 cm in greatest dimension, limited to the kidney
- cT2a Tumour more than 7 cm but not more than 10 cm
- cT2b Tumour more than 10 cm, limited to the kidney

cT3 Tumour extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota fascia
- cT3a Tumour extends into the renal vein or its segmental branches, or tumour invades the pelvicalyceal system or tumour invades perirenal and/or renal sinus fat (peripelvic) fat but not beyond Gerota fascia
- cT3b Tumour extends into vena cava below diaphragm
- cT3c Tumour extends into vena cava above the diaphragm or invades the wall of the vena cava

cT4 Tumour invades beyond Gerota fascia (including contiguous extension into the ipsilateral adrenal gland)

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in regional lymph node(s)

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1, T2, T3	N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

Prognostic Factors Grid – Kidney

Prognostic factors for cancers of the kidney

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM	Age Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Histological subtype and grade. Presence of sarcomatoid or rhabdoid features LV invasion necrosis	Performance status Serum LDH, calcium Haemoglobin, neutrophils and platelets Hereditary syndromes	Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.
Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang.

Renal Pelvis and Ureter
(ICD-O-4 C65, C66)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to carcinomas. Papilloma and papillary urothelial neoplasm of low malignant potential (PUNLM) are excluded. There should be histological or cytological confirmation of the disease.

Anatomical Sites

1. Renal pelvis (C65)
2. Ureter (C66)

Regional Lymph Nodes

The regional lymph nodes are the hilar, abdominal para-aortic and paracaval nodes and, for ureter, intrapelvic nodes. Laterality does not affect the N classification.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTa Non-invasive papillary carcinoma
cTis Carcinoma in situ

cT1 Tumour invades subepithelial connective tissue
cT2 Tumour invades muscularis
cT3 (*Renal pelvis*) Tumour invades beyond muscularis into peripelvic fat or renal parenchyma
(*Ureter*) Tumour invades beyond muscularis into periureteric fat
cT4 Tumour invades adjacent organs or through the kidney into perinephric fat

cN – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single lymph node 2 cm or less in greatest dimension
cN2 Metastasis in a single lymph node more than 2 cm or multiple lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage IV	T4	N0	M0
	Any T	N1, N2	M0
	Any T	Any N	M1

Urinary Bladder
(ICD-O-4 C67)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to carcinomas. Papilloma and papillary urothelial neoplasm of low malignant potential (PUNLMP) are excluded. There should be histological or cytological confirmation of the disease.

Regional Lymph Nodes

The regional lymph nodes are the nodes of the true pelvis, which essentially are the pelvic nodes below the bifurcation of the common iliac arteries. Laterality does not affect the N classification.

TNM Clinical Classification

T – Primary Tumour

The suffix (m) should be added to the appropriate T category to indicate multiple tumours. The suffix (is) may be added to any T to indicate the presence of associated carcinoma in situ.

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTa Non-invasive papillary carcinoma
cTis Carcinoma in situ: 'flat tumour'

cT1 Tumour invades subepithelial connective tissue
cT2 Tumour invades muscularis propria
- cT2a Tumour invades superficial muscularis propria (inner half)
- cT2b Tumour invades deep muscularis propria (outer half)

cT3 Tumour invades perivesical tissue:
- cT3a microscopically
- cT3b macroscopically (extravesical mass)

cT4 Tumour invades any of the following: prostate stroma, seminal vesicles, uterus, vagina, pelvic wall or abdominal wall
- cT4a Tumour invades prostate stroma, seminal vesicles, uterus or vagina
- cT4b Tumour invades pelvic wall or abdominal wall

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single lymph node in the true pelvis (hypogastric, obturator, external iliac or presacral)
cN2 Metastasis in multiple regional lymph nodes in the true pelvis (hypogastric, obturator, external iliac or presacral)
cN3 Metastasis in a common iliac lymph node(s)

M – Distant Metastasis

M0 No distant metastasis
M1a Non-regional lymph nodes
M1b Other distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2a, T2b	N0	M0
Stage IIIA	T3a, T3b, T4a	N0	M0
	T1, T2, T3, T4a	N1	M0
Stage IIIB	T1, T2, T3, T4a	N2, N3	M0
Stage IVA	T4b	Any N	M0
	Any T	Any N	M1a
Stage IVB	Any T	Any N	M1b

Prognostic Factors Grid – Bladder

Prognostic factors for metastatic risk and survival in invasive, locally-advanced and/or node positive bladder cancer (T2–4 N0–1)

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM	Age Performance status ALP Other co-morbidities	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Grade, Histology Lymphovascular invasion Concomitant Cis Multifocality Tumour size R status Hydronephrosis FGFR3 genetic alteration HER2, PD-L1 expression	Haemoglobin Response of primary to chemotherapy?	Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information R status

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Urethra
(ICD-O-4 C68.0, C61.9)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

The classification applies to carcinomas of the urethra (ICD-O-4 C68.0) and urothelial carcinomas of the prostate (ICD-O-4 C61.9) and prostatic urethra. There should be histological or cytological confirmation of the disease.

Regional Lymph Nodes

The regional lymph nodes are the inguinal and the pelvic nodes. Laterality does not affect the N classification.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

Urethra (male and female)

cTa Non-invasive papillary, polypoid or verrucous carcinoma
cTis Carcinoma in situ

cT1 Tumour invades subepithelial connective tissue
cT2 Tumour invades any of the following: corpus spongiosum, prostate or periurethral muscle
cT3 Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule, anterior vagina or bladder neck (extraprostatic extension)
cT4 Tumour invades other adjacent organs (invasion of the bladder)

Urothelial carcinoma of the prostate and prostatic urethra

cTis Carcinoma in situ, involving the prostatic urethra, periurethral or prostatic ducts without stromal invasion

cT1 Tumour invades subepithelial connective tissue (for tumours involving prostatic urethra only)
cT2 Tumour invades any of the following: prostatic stroma, corpus spongiosum or periurethral muscle
cT3 Tumour invades any of the following: corpus cavernosum, beyond prostatic capsule or bladder neck (extraprostatic extension)
cT4 Tumour invades other adjacent organs (invasion of the bladder or rectum)

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in a single lymph node
cN2 Metastasis in multiple lymph nodes

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2	N1	M0
	T3	N0, N1	M0
Stage IV	T4	N0, N1	M0
	Any T	N2	M0
	Any T	Any N	M1

Adrenal Cortex

(ICD-O-4 C74.0)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

This classification applies only to carcinomas of the adrenal cortex. It does not apply to tumours of the adrenal medulla or sarcomas.

Regional Lymph Nodes

The regional lymph nodes are the hilar, abdominal para-aortic and paracaval nodes. Laterality does not affect the N categories.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cT1 Tumour 5 cm or less in greatest dimension, no extra-adrenal invasion
cT2 Tumour greater than 5 cm, no extra-adrenal invasion
cT3 Tumour of any size with local invasion, but not invading adjacent organs*
cT4 Tumour of any size with invasion of adjacent organs*

Note

* Adjacent organs include kidney, diaphragm, great vessels (renal vein or vena cava), pancreas and liver.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Metastasis in regional lymph node(s)

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

M – Distant Metastasis

cM0 No distance metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the T and N categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2	N1	M0
	T3, T4	N0, N1	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid

Prognostic factors for survival in adrenal cortical carcinoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Function Grade Ki67 R status	Age Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Capsular invasion, venous invasion and sinusoidal invasion. Molecular markers, IGF-1		Expertise of a treatment at the specific level (e.g., surgery) Access to information R status after surgery

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Adrenal Medulla and Extra-Adrenal Paraganglia Tumours

(ICD-O-4 C74.1, C75.5)

The definitions of the T, N and M categories correspond to the AJCC 8th edition/version.

Rules for Classification

This classification applies to paraganglion neuroendocrine tumours, consisting of phaeochromocytomas of the adrenal medulla (C74.1) and paragangliomas[a] of the aortic body and other paragangliomas (C75.5). Carotid body tumours are excluded.[b]

Notes

[a] Sympathetic paragangliomas are functional.

[b] Parasympathetic paragangliomas are non-functional and are commonly found in the head and neck region (i.e., carotid body tumours) and usually have an excellent prognosis.

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Regional Lymph Nodes

The regional lymph nodes are para-aortic and retroperitoneal nodes for pelvic and abdominal paragangliomas/phaeochromocytomas and para-aortic and posterior mediastinum for thoracic paragangliomas.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Phaeochromocytoma 5 cm or less in greatest dimension, no extra-adrenal invasion
cT2 Phaeochromocytoma greater than 5 cm in greatest dimension, no extra-adrenal invasion
Paraganglioma[a] of any size, no local invasion
cT3 Tumour of any size with local invasion, into adjoining tissues or adjacent organs[a]

Notes

[a] Adjacent organs include kidney, liver, pancreas and spleen.

There is no cT4.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distance metastasis
cM1 Distance metastasis
cM1a Bone only
cM1b Distant sites excluding bone
cM1c Bone and other distant sites

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T1, T2	N1	M0
	T3	N0, N1	M0
Stage IV	Any T	Any N	M1

Ophthalmic Tumours

Introductory Notes

Tumours of the eye and its adnexa are a disparate group including carcinoma, melanoma, sarcomas and retinoblastoma. For clinical convenience, they are classified in one section.

The following sites are included:

- Conjunctiva
- Uvea
- Retina
- Orbit
- Lacrimal gland

Eyelid (eyelid tumours are classified with skin tumours, see page 141).

For histological nomenclature and diagnostic criteria, reference to the WHO histological classification is recommended.[1]

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Carcinoma of Conjunctiva
(ICD-O-4 C69.0)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

There should be histological confirmation of the disease and division of cases by histological type, for example, mucoepidermoid and squamous cell carcinoma.

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

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

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Carcinoma in situ
cT1 Tumour 5 mm or less in greatest dimension invades through the conjunctival basement membrane
cT2 Tumour more than 5 mm in greatest dimension, invades through the conjunctival basement membrane without invasion of adjacent structures*
cT3 Tumour invades adjacent structures*
cT4 Tumour invades the orbit or beyond
- cT4a Tumour invades orbital soft tissues, without bone invasion
- cT4b Tumour invades bone
- cT4c Tumour invades adjacent paranasal sinuses
- cT4d Tumour invades brain

Note

* Adjacent structures include the cornea (3, 6, 9 or 12 clock hours), intraocular compartments, forniceal conjunctiva (lower and/or upper), palpebral conjunctiva (lower and/or upper), tarsal conjunctiva (lower and/or upper), lacrimal punctum and canaliculi (lower and/or upper), plica, caruncle, posterior eyelid lamella, anterior eyelid lamella and/or eyelid margin (lower and/or upper).

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

No stage is at present recommended.

Melanoma of Conjunctiva
(ICD-O-4 C69.0)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies only to conjunctival melanoma. There should be histological confirmation of the disease.

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

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

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour
cTis Melanoma confined to the conjunctival epithelium (in situ)[a]

cT1 Melanoma of the bulbar conjunctiva
- cT1a Tumour involves less than or equal to one quadrant[b]
- cT1b Tumour involves more than one but less than or equal to two quadrants
- cT1c Tumour involves more than two but less than or equal to three quadrants
- cT1d Tumour involves more than three quadrants

cT2 Melanoma of the non-bulbar conjunctiva involving palpebral, forniceal and/or caruncular conjunctiva
- cT2a Non-caruncular tumour involves less than or equal to one quadrant
- cT2b Non-caruncular tumour involves more than one quadrant
- cT2c Caruncular tumour involves less than or equal to one quadrant of conjunctiva
- cT2d Caruncular tumour involves more than one quadrant of conjunctiva

cT3 Tumour with local invasion into:
- cT3a Globe
- cT3b Eyelid
- cT3c Orbit
- cT3d Paranasal sinus, nasolacrimal duct and/or lacrimal gland

cT4 Tumour invades central nervous system

Notes

[a] Melanoma in situ (includes the term primary acquired melanosis) with atypia replacing greater than 75% of the normal epithelial thickness with cytological features of epithelial cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, and/or presence of intraepithelial nest of atypical cells.

[b] Quadrants are defined by clock hour, starting at the limbus (e.g., 6, 9, 12, 3) extending from the central cornea, to and beyond the eyelid margins. This will bisect the caruncle.

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

pT – Primary Tumour

pTX Primary tumour cannot be assessed
pT0 No evidence of primary tumour
pTis Melanoma confined to the conjunctival epithelium (in situ)*

pT1 Melanoma of the bulbar conjunctiva
- pT1a Tumour 2.0 mm or less in thickness with invasion of the substantia propria
- pT1b Tumour more than 2.0 mm in thickness with invasion of the substantia propria

pT2 Melanoma of the palpebral, forniceal or caruncular conjunctiva
- pT2a Tumour 2.0 mm or less in thickness with invasion of the substantia propria
- pT2b Tumour more than 2.0 mm in thickness with invasion of the substantia propria

pT3 Melanoma invades the eye, eyelid, nasolacrimal system or orbit
- pT3a Invades the globe
- pT3b Invades the eyelid
- pT3c Invades the orbit
- pT3d Invades the paranasal sinus and/or nasolacrimal duct or lacrimal sac

pT4 Melanoma invades central nervous system

Note

* pTis Melanoma in situ (includes the term primary acquired melanosis) with atypia replacing greater than 75% of the normal epithelial thickness, with cytological features of epithelioid cells, including abundant cytoplasm, vesicular nuclei or prominent nucleoli, and/or presence of intraepithelial nests of atypical cells.

pN – Regional Lymph Nodes

The pN categories correspond to the N categories.

pM – Distant Metastasis

For pM categories, see page 8.

G – Histopathological Grading

Histological grade represents the origin of the primary tumour.

GX Origin cannot be assessed
G0 Primary acquired melanosis without cellular atypia
G1 Conjunctival nevus
G2 Primary acquired melanosis with cellular atypia (epithelial disease only)
G3 Primary acquired melanosis with epithelial cellular atypia and invasive melanoma
G4 De novo malignant melanoma

Stage

No stage is at present recommended.

Melanoma of Uvea
(ICD-O-4 C69.3-4)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

There should be histological confirmation of the disease.

The following are the procedures for assessing T, N and M categories.

Regional Lymph Nodes

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

Anatomical Sites

1. Iris (C69.4)
2. Ciliary body (C69.4)
3. Choroid (C69.3)

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

Iris*

cT1 Tumour limited to iris
- cT1a not more than 3 clock hours in size
- cT1b more than 3 clock hours in size
- cT1c with secondary glaucoma

cT2 Tumour confluent with or extending into the ciliary body, choroid or both
- cT2a Tumour confluent with or extending into the ciliary body without secondary glaucoma
- cT2b Tumour confluent with or extending into the choroid without secondary glaucoma
- cT2c Tumour confluent with or extending into the ciliary body and/or choroid with secondary glaucoma

cT3 Tumour confluent with or extending into the ciliary body, choroid or both, with scleral extension

cT4 Tumour with extrascleral extension
- cT4a less than or equal to 5 mm in diameter
- cT4b more than 5 mm in diameter

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.

Ciliary Body and Choroid

Primary ciliary body and choroidal melanomas are classified according to the four tumour size categories listed in this section[a,b] (Figure 1).

cT1 Tumour size category 1
- cT1a without ciliary body involvement and extraocular extension
- cT1b with ciliary body involvement
- cT1c without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter
- cT1d with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter

cT2 Tumour size category 2
- cT2a without ciliary body involvement and extraocular extension
- cT2b with ciliary body involvement
- cT2c without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter
- cT2d with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter

cT3 Tumour size category 3
- cT3a without ciliary body involvement and extraocular extension
- cT3b with ciliary body involvement
- cT3c without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter

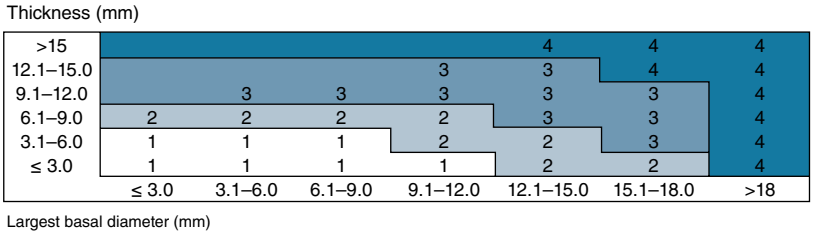

Figure 1 Classification for ciliary body and choroid uveal melanoma based on thickness and diameter.

cT3d with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter

cT4 Tumour size category 4

- cT4a without ciliary body involvement and extraocular extension
- cT4b with ciliary body involvement
- cT4c without ciliary body involvement but with extraocular extension less than or equal to 5 mm in diameter
- cT4d with ciliary body involvement and extraocular extension less than or equal to 5 mm in diameter
- cT4e Any tumour size category with extraocular extension more than 5 mm in diameter

Notes

[a] In clinical practice, the largest tumour basal diameter may be estimated in optic disc diameters (dd, average: 1 dd = 1.5 mm). Tumour thickness may be estimated in diopters (average: 2.5 diopters = 1 mm). However, techniques such as ultrasonography and fundus photography are used to provide more accurate measurements. Ciliary body involvement can be evaluated by the slit-lamp, ophthalmoscopy, gonioscopy and transillumination. However, high-frequency ultrasonography (ultrasound biomicroscopy) is used for more accurate assessment. Extension through the sclera is evaluated visually before and during surgery, and with ultrasonography, computed tomography or magnetic resonance imaging.

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

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

- cM1a Largest metastasis 3 cm or less in greatest dimension
- cM1b Largest metastasis is larger than 3 cm in greatest dimension but not larger than 8 cm
- cM1c Largest metastasis is larger than 8 cm in greatest dimension

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage*

Stage I	T1a	N0	M0
Stage IIA	T1b–d, T2a	N0	M0
Stage IIB	T2b, T3a	N0	M0
Stage IIIA	T2c–d	N0	M0
	T3b–c	N0	M0
	T4a	N0	M0
Stage IIIB	T3d	N0	M0
	T4b–c	N0	M0
Stage IIIC	T4d–e	N0	M0
Stage IV	Any T	N1	M0
	Any T	Any N	M1

Note

* The stage groups are for malignant melanoma of the choroid and ciliary body but not of the iris.

Prognostic Factors Grid

Prognostic factors for survival for uveal melanoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Largest tumour diameter (typically width)	Age Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status Screening
Additional	Extrascleral 'extraocular' extension Location Histopathological cell type Mitotic activity Microvasculature patterns	HLA Tissue type – HLA-A*02:01–positive	Expertise of a treatment at the specific level Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Retinoblastoma
(ICD-O-4 C69.2)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/ version.

Rules for Classification

In bilateral cases, the eyes should be classified separately. The classification does not apply to complete spontaneous regression of the tumour. There should be histological confirmation of the disease in an enucleated eye.

For Retinoblastoma in paediatric patients, please also see page 247.

Regional Lymph Nodes

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

Additional Descriptor:

Heritable Trait Classification (H)

The H classification identifies patients with germline cancer predisposition and consequently risk of subsequent new primaries and second malignancies such as cutaneous melanoma and osteosarcoma

HX Unknown or insufficient evidence of a constitutional RB! Gene mutation
H0 Normal RBI alleles tested with high sensitivity assay
H1 Constitutional RB1 gene mutation, or,
Bilateral retinoblastoma
Trilateral retinoblastoma (retinoblastoma and an intracranial primitive neuroectodermal tumour)
Family history of retinoblastoma

Note
The stage is not altered.

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed.
cT0 No evidence of primary tumour.

cT1 Tumour confined to the retina with subretinal fluid not more than 5 mm from the base of any tumour, without retinal detachment
- cT1a No tumour in either eye is greater than 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea
- cT1b At least one tumour is greater than 3 mm in largest dimension or located closer than 1.5 mm to the optic nerve or fovea. No retinal detachment or subretinal fluid beyond 5 mm from the base of the tumour

cT2 Tumours with vitreous or subretinal seeding or retinal detachment
- cT2a Tumour with subretinal fluid more than 5 mm from the base of any tumour
- cT2b Tumour with vitreous and/or subretinal seeding

cT3 Severe intraocular disease
- cT3a Phthisis or prephthisis bulbi
- cT3b Invasion of choroid, pars plana, ciliary body, lens, zonules, iris or anterior chamber
- cT3c Raised intraocular pressure with neovascularisation and/or buphthalmos
- cT3d Hyphema and/or massive vitreous haemorrhage
- cT3e Aseptic orbital cellulitis

cT4 Extraocular tumour
- cT4a Invasion of optic nerve or orbital tissues
- cT4b Extraocular invasion with proptosis and/or orbital mass

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis
- M1a Single or multiple metastasis to sites other than CNS or brain
- M1b Metastasis to the CNS including brain

TNM Pathological Classification

T – Primary Tumour

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

pT1 Tumour confined to eye with no optic nerve or choroidal invasion
pT2 Tumour with intraocular invasion
- pT2a Focal choroidal invasion and pre- or intralaminar invasion of the optic nerve head
- pT2b Tumour invasion of stroma of iris and/or trabecular meshwork and/or Schlemm canal

pT3 Tumour with significant local invasion
- pT3a Choroidal invasion larger than 3 mm in diameter or multiple foci of invasion totalling more than 3 mm or any full-thickness involvement
- pT3b Retrolaminar invasion of optic nerve without invasion of transected end of optic nerve
- pT3c Partial-thickness involvement of sclera within the inner two-thirds
- pT3d Full-thickness invasion into outer third of the sclera and/or invasion into or around emissary channels

pT4 Extraocular extension: Tumour invades optic nerve at transected end, in meningeal space around the optic nerve, full-thickness invasion of the sclera with invasion of the episclera, adipose tissue, extraocular muscle, bone, conjunctiva or eyelid.

N – Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node involvement
pN1 Regional lymph node involvement

pM – Metastasis

cM0 No distant metastasis
pM1 Distant metastasis
pM1a Single or multiple metastasis to sites other than CNS
pM1b Metastasis to CNS parenchyma or cerebrospinal fluid

Stage

Clinical stage

Stage I	T1, T2, T3	N0	M0
Stage II	T4a	N0	M0
Stage III	T4b	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

Pathological Stage

Stage I	T1, T2, T3	N0	M0
Stage II	T4	N0	M0
Stage III	Any T	N1	M0
Stage IV	Any T	Any N	M1

Prognostic Factors Grid

Prognostic factors for survival for retinoblastoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	TNM Massive = > or equal to 3-mm′ uveal invasion Extrascleral tumour extension Optic nerve invasion Anterior chamber extension	Age Immunosuppression Germline mutation *RB1* allele	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status Screening
Additional	Multidrug resistance gene(s) Heritability		Expertise of a treatment at the specific level Telepathology *In utero* detection of Rb Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

Source: Adapted from: UICC Manual of Clinical Oncology, Ninth Edition. Edited by Brian O'Sullivan, James D. Brierley, Anil K. D'Cruz, Martin F. Fey, Raphael Pollock, Jan B. Vermorken and Shao Hui Huang. © 2015 UICC. Published 2015 by John Wiley & Sons, Ltd.

Sarcoma of Orbit
(ICD-O-4 C69.6)

The definitions of the T, N and M categories correspond with the AJCC 8th edition/version.

Rules for Classification

The classification applies to sarcomas of soft tissue and bone. There should be histological confirmation of the disease and division of cases by histological type.

Regional Lymph Nodes

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

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour 20 mm or less in greatest dimension
cT2 Tumour more than 20 mm in greatest dimension without invasion of globe or bony wall
cT3 Tumour of any size with invasion of orbital tissues and/or bony walls
cT4 Tumour invades globe or periorbital structure, such as eyelids, temporal fossa, nasal cavity and paranasal sinuses, and/or central nervous system

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

No stage is at present recommended.

Carcinoma of Lacrimal Gland
(ICD-O-4 C69.5)

Rules for Classification

There should be histological confirmation of the disease and division of cases by histological type.

Regional Lymph Nodes

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

TNM Clinical Classification

T – Primary Tumour

cTX Primary tumour cannot be assessed
cT0 No evidence of primary tumour

cT1 Tumour 2 cm or less in greatest dimension, with or without extraglandular extension into the orbital soft tissue
- cT1a No periosteal or bone involvement
- cT1b Periosteal involvement without bone involvement
- cT1c Bone involvement

cT2 Tumour more than 2 cm but not more than 4 cm in greatest dimension.
- cT2a No periosteal or bone involvement
- cT2b Periosteal involvement without bone involvement

cT2c Bone involvement

cT3 Tumour more than 4 cm or with extraglandular extension into orbital soft tissue, including optic nerve, or globe
- cT3a No periosteal or bone involvement
- cT3b Periosteal involvement without bone involvement
- cT3c Bone involvement

cT4 Tumour invades adjacent structures (sinuses, temporal fossa, pterygoid fossa, superior orbital fissure, cavernous sinus and/or brain)
- cT4a Not more than 2 cm in greatest dimension
- cT4b More than 2 cm but not more than 4 cm in greatest dimension
- cT4c More than 4 cm in greatest dimension

N – Regional Lymph Nodes

cNX Regional lymph nodes cannot be assessed
cN0 No regional lymph node metastasis
cN1 Regional lymph node metastasis

M – Distant Metastasis

cM0 No distant metastasis
cM1 Distant metastasis

pTNM Pathological Classification

The pT and pN categories correspond to the cT and cN categories, respectively. For pM, see page 8.

Stage

No stage is at present recommended.

Reference

1 *WHO Classification of Tumours of the Eye*, vol. 13, 5th Edition, Lyon (France): International Agency for Research on Cancer, 2023. https://tumourclassification.iarc.who.int.

Brain and Spinal Cord

(ICD-O-4 C71, C72.0-C72.1, C75.3)

The definitions of the T, N and M categories correspond with the AJCC 9th version.

Rules for Classification

The classification applies only to medulloblastomas, medulloepithelioma, CNS embryonal tumour, atypical teratoid/rhabdoid tumour and pineoblastoma. There should be histological confirmation of the disease and division of cases by histological type.
For paediatric patients, please see page 249.

Regional Lymph Nodes

There are no regional lymph nodes.

TNM Clinical Classification

T – Primary Tumour

Not applicable for brain and spinal cord tumours.

N – Regional Lymph Nodes

Not applicable for brain and spinal cord tumours.

M – Distant Metastasis

TNM categories	Modified Chang stages[1,2]	Definition
cM0	M0	No distant metastasis
cM1		Distant metastasis
cM1b	M2	Intracranial spread beyond primary site
cM1c	M3	Gross spinal subarachnoid seeding on MRI
cM1d	M4	Metastasis outside CNS (bone marrow, lungs)

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pTNM Pathological Classification

pT – Primary Tumour

Not applicable for brain and spinal cord tumours.

pN – Regional Lymph Nodes

Not applicable for brain and spinal cord tumours.

M – Distant Metastasis

TNM categories	Modified Chang stages[1,2] definition	
pM1		Distant metastasis
pM1a	M1	Microscopic confirmation of tumour cells present in cerebrospinal fluid (CSF) by cytology
pM1b	M2	Microscopic confirmation intracranial spread beyond primary site
pM1c	M3	Microscopic confirmation of gross spinal subarachnoid seeding
pM1d	M4	Microscopic confirmation of metastasis outside CNS (bone marrow, lungs)

Stage

No stage is at present recommended.

References

1 Harisiadis L, Chang CH. Medulloblastoma in children: a correlation between staging and results of treatment. Int J Radiat Oncol Biol Phys 1977;2(9–10):833–841.
2 Chang CH, Housepian EM, Herbert C, Jr. An operative staging system and a megavoltage radiotherapeutic technic for cerebellar medulloblastomas. Radiology 1969;93(6):1351–1359.

Hodgkin Lymphoma

Introductory Notes

The current staging classification for Hodgkin Lymphoma is a modification of the Ann Arbor classification first adopted in 1971. Over the past 45 years, the practice has changed, making the previously used staging laparotomy and the resulting pathological staging classification obsolete. The recent consensus conference that took place in 2012 in Lugano suggested even more simplified system putting together stages I and II as Limited Stage and stages III and IV as Advanced Stage lymphoma. The Lugano Classification, a modification of the Ann Arbor classification, has been published and accepted by the UICC.[1]

Clinical Staging (cS)

It is determined by history, clinical examination, imaging, blood analysis and the initial biopsy report. Bone marrow biopsy must be taken from a clinically or radiologically non-involved area of bone.

Liver Involvement

Clinical evidence of liver involvement must include either enlargement of the liver and at least an abnormal serum alkaline phosphatase level and two different liver function test abnormalities or an abnormal liver demonstrated by imaging and one abnormal liver function test.

Spleen Involvement

Clinical evidence of spleen involvement is accepted if there is palpable enlargement of the spleen confirmed by imaging.

Lymphatic and Extralymphatic Disease

The lymphatic structures are as follows:

- Lymph nodes
- Waldeyer ring
- Spleen
- Appendix
- Thymus
- Peyer patches

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The lymph nodes are grouped into regions and one or more (2, 3, etc.) may be involved. The spleen is designated S and extralymphatic organs or sites E.

Lung Involvement

Lung involvement limited to one lobe, or perihilar extension associated with ipsilateral lymphadenopathy, or unilateral pleural effusion with or without lung involvement but with hilar lymphadenopathy is considered as **localised** extralymphatic disease.

Liver Involvement

Liver involvement is always considered as **diffuse** extralymphatic disease.

Clinical Stages (cS)

Limited Stage

Stage I

Involvement of a single lymph node region (I) or localised involvement of a single extralymphatic organ or site (IE).

Stage II

Involvement of two or more lymph node regions on the same side of the diaphragm (II), or localised involvement of a single extralymphatic organ or site and its regional lymph node(s) with or without involvement of other contiguous lymph node regions on the same side of the diaphragm (IIE).

Bulky Stage II

Stage II disease with a single nodal mass greater than 10 cm in maximum dimension or greater than a third of the thoracic diameter as assessed on CT.

Advanced Stage

Stage III

Involvement of lymph node regions on both sides of the diaphragm (III), which may also be accompanied by involvement of the spleen (IIIS).

Stage IV

Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or non-contiguous extralymphatic organ involvement with involvement of lymph node regions on the same or both sides of the diaphragm.

A and B Classification (Symptoms)

Each stage should be divided into A and B according to the absence or presence of defined general symptoms. These are:

1. Unexplained weight loss of more than 10% of the usual body weight in the 6 months prior to first attendance

2. Unexplained fever with temperature above 38 °C
3. Night sweats

Note

Pruritus alone does not qualify for B classification nor does a short, febrile illness associated with a known infection.

Prognostic Factors Grid for Hodgkin Disease

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Limited or extensive Histology/subtypes Bulky mediastinal disease or bulky disease greater than 10 cm Number of involved nodes B symptoms Extranodal disease: ESR	Age Sex Performance status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	Albumin level below 4 g/dL Low haemoglobin level High white blood cell count Lymphocyte count Early metabolic response with FDG-PET scan		Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information

* See page 12 for a more complete list of environmental and social determinants of health factors.

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Reference

1 Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol* 2014; 32: 3059–3068.

Non-Hodgkin Lymphomas

The Lugano classification, a modification of the Ann Arbor classification, is recommended as for Hodgkin lymphoma with the exception of the elimination of the A or B classification of symptoms (see page 228).

In Stage II disease, bulk is defined as larger than 6 cm in greatest dimension in follicular lymphoma, and 10 cm in largest dimension has been recommended for diffuse large cell lymphoma.

For Non-Hodgkin Lymphoma in paediatric patients, the St Jude/Murphy system is recommended (see page 247).

Prognostic Factors Grid Diffuse Large B Cell Lymphoma

Prognostic factors	Tumour related	Host related	Environment related*
Essential	Extensive extranodal involved Tumour bulk B symptoms LDH International prognostic index	Age Sex Performance status Immune deficiency status	Distance from treatment centre Access to specific investigations and/or treatments Socioeconomic status
Additional	WHO classification of haematolymphoid tumours (WHO-HAEM5) Gene expression profiling (GEP) germinal centre B-cell-like (GCB-like) and activated B-cell-like (ABC-like) Cell of origin (COO)	HIV status Hepatitis B and C Status	Expertise of a treatment at the specific level (medical oncology or radiotherapy) Access to information

(Continued)

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

(Continued)

Prognostic factors	Tumour related	Host related	Environment related*
	Genomic expression Beta-2-microglobulin Lymphocyte-to-monocyte ratio		

* See page 12 for a more complete list of environmental and social determinants of health factors.

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Primary Cutaneous Lymphomas

Primary cutaneous lymphoma was not included in the previous eighth edition TNM Classification but were included in the fifth edition supplement. Subsequently, the International Society for Cutaneous Lymphoma (ICLS), the United States Cutaneous Lymphoma Consortium (USCLC), and the Cutaneous Lymphoma Task Force of the European Organization for the Research and Treat of Cancer (EORTC) have recently published updated staging and guidelines for the management of cutaneous lymphoma. The recommendations for staging are summarised below. For more information regarding the staging of primary cutaneous lesions and their response to treatment, please see:

Olsen E, Whittaker S, Willemze, et al. Primary cutaneous lymphoma: recommendations for clinical trial design and staging update from the ISCL, USCLC, and EORTC. *Blood* 2022; 140 (5): 419–437. https://doi.org/10.1182/blood.2021012057

The tables below are adapted.

Rules for Classification

The classification applies to primary cutaneous lymphoma, mycosis fungoides (MF), Sézary syndrome (SS) and T and B Cell Cutaneous Lymphoma.

There should be histological confirmation of the disease.

Anatomical Sites

The following sites are identified by the ICD-O topography rubrics:

1. External ear and other parts of face (excluding lip and eyelid) (C44. 2–3)
2. Scalp and neck (C44.4)
3. Trunk (including anal margin and perianal skin) (C44.5, C21.3)
4. Arm and shoulder (C44.6)
5. Leg and hip (C44.7)

6. Labium majus and minus, clitoris and vulva (C51. 0–2, 8–9)
7. Prepuce, glans penis, body of penis and penis (C60. 0–2, 8–9)
8. Scrotum (C63.2)

Regional Lymph Nodes

The regional lymph nodes are the superficial nodes, i.e., those of head and neck (preauricular, submandibular, cervical), and the axillary, epitrochlear, inguinal and popliteal nodes.

Primary Cutaneous Lymphomas

The tables are adapted from Olsen E, Whittaker S, Willemze, et al. Primary cutaneous lymphoma: recommendations for clinical trial design and staging update from the ISCL, USCLC, and EORTC. *Blood* 2022; 140 (5): 419–437. https://doi.org/10.1182/blood.2021012057.

T and B Cutaneous Lymphoma (non-Mycosis Fungoides or Sézary syndrome)

T – Primary Tumour

T1 Solitary lesion
- T1a <5 cm in diameter
- T1b ≥5 cm in diameter

T2 Multiple lesions limited to one body region or two contiguous body regions
- cT2a All disease <15 cm in diameter
- cT2b All disease ≥15 cm to <30 cm in diameter
- cT2c All disease ≥30 cm in diameter without extending beyond 2 contiguous body regions

T3 Generalised disease
- cT3a Multiple lesions involving two non-contiguous body lesions
- cT3b Three or more body regions involved

N – Regional Lymph Nodes

N0 No clinically abnormal peripheral lymph nodes
N1 Involvement of 1 peripheral nodal region that drains the area of involved skin
N2 Involvement of ≥ 2 peripheral node regions or involvement of any node region that does not drain the area of involved skin
N3 Involvement of central node on biopsy

M – Distant Metastasis

M0 No visceral involvement
M1 M1 Visceral involvement

Stage

There is no stage.

Mycosis Fungoides or Sézary syndrome

Note this is a prognostic group as the N category is histopathology findings and T-Cell Clone. In addition, the prognostic group is also determined by the absence or presence of peripheral blood involvement.

T – Primary Tumour

T1 Limited patches, papules, and/or plaques covering < 10% of the skin surface
- T1a Patch only
- T1b Plaque/papule ± patch

T2 Patches, papules, or plaques covering ≥10% of the skin surface
- T2a Patch only
- T2b Plaque/papule ± patch

T3 One or more tumours (≥1 cm in diameter)

T4 Confluence of erythema covering ≥80% of the body surface area

N – Regional Lymph Nodes

NX Clinically abnormal peripheral lymph nodes, no histologic confirmation

N0 No clinically abnormal peripheral lymph nodes*, biopsy not required

N1 Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 1 or National Cancer Institute (NCI) LN0-2
- pN1a Clone negative** or equivocal
- pN1b Clone positive** and identical to skin

N2 Clinically abnormal peripheral lymph nodes; histopathology Dutch grade 2 or NCI LN3
- pN2a Clone negative** or equivocal
- pN2b Clone positive** and identical to skin

N3 Clinically abnormal peripheral lymph nodes; Histopathology Dutch grades 3–4 or NCI LN4; pN3a Clone negative** or equivocal
- pN3b Clone positive** and identical to skin

Notes

* A lymph node (LN) of >1.5 cm in the longest diameter (LDi) is considered abnormal, especially if accompanied by other features of concern (firm, rubbery and/or fixed) but should be confirmed by imaging. Central nodes, which generally are not amenable to pathological assessment, currently are not considered in the nodal classification unless used to establish N3 histopathologically.

** A T cell clone is defined by polymerase chain reaction (PCR) or Southern blot analysis of the TCR genes.

M – Metastasis

M0 No visceral organ involvement
M1a Bone Marrow only
  M1a1 Clone negative* or equivocal
  M1a2 Clone positive* and identical to skin
M1b Non-bone marrow visceral involvement with or without bone marrow involvement
  M1b1 Clone negative* or equivocal
  M1b2 Clone positive* and identical to skin

Note

* For viscera, spleen and liver may be diagnosed b imaging criteria.

Histopathologic staging of lymph nodes in mycosis fungoides and Sézary syndrome

EORTC classification	Dutch system	NCI-VA classification
N1	Grade 1: Dermatopathic lymphadenopathy (DL)	LN0: No atypical lymphocytes
		LN1: Occasional and isolated Atypical Lymphocytes (not arranged in clusters)
		LN2: Many atypical lymphocytes or lymphocytes in 3–6 cell clusters
N2	Grade 2: DL; early involvement b MF (presence of cerebriform nuclei <7.5 μm)	LN3: Aggregates of atypical lymphocytes; nodal architecture preserved
N3	Grade 3: partial effacement of lymph node architecture; many atypical cerebriform architecture by atypical lymphocytes mononuclear cells	LN4: Partial/complete effacement of nodal or frankly neoplastic cells
	Grade 4: complete effacement	

Peripheral Blood Involvement (B)

B category	B criteria
B0	Absence of significant blood involvement: ≤250/μL of $CD4^+$/$CD26^-$ or $CD4^+$/$CD7^-$ cells
	B0a Clone negative*
	B0b Clone positive*
B1	Low blood tumour burden: >250/μL but ≤1000/μL of $CD4^+$/$CD26^-$ or $CD4^+$/$CD7^-$ cells
	B1a Clone negative*
	B1b Clone positive
B2	High blood tumour burden: ≥1000/μL of $CD4^+$/$CD26^-$ or $CD4^+$/$CD7^-$ cells or other aberrant population of lymphocytes identified by flow cytometry

Prognostic Group – Mycosis Fungoides and Sézary Syndrome

IA	T1	N0	M0	B0, B1
IB	T2	N0	M0	B0, B1
IIA	T1, 2	N1-2	M0	B0, B1
IIB	T3	N0-2	M0	B0, B1
III	T4	N0-2	M0	B0, B1
IIIa	T4	N0-2	M0	B0
IIIb	T4	N0-2	M0	B1
IVa1	Any T	N0-2	M0	B2
IVa2	Any T	N3	M0	Any B
IVb	Any T	Any N	M1	Any B

Essential TNM

Information on the anatomical extent of disease or stage at presentation is central to cancer surveillance to establish cancer burden as it provides additional valuable information to incidence, survival and mortality data. However, cancer registries particularly in low- and middle-income countries frequently have insufficient information to determine complete TNM data either because of inability to perform necessary investigations or because of lack of recording of information. In view of this, the UICC TNM Project has with the International Agency for Research in Cancer developed 'Essential TNM' that can be used to collect stage data by cancer registrars, when complete TNM information is not available. Essential TNM flow-charts were originally developed for breast, cervix, colon and prostate carcinomas and have been expanded to now include also oesophageal, hepatocellular, ovarian carcinomas and lymphomas. The Essential TNM User's Guide is available for download at https://publications.iarc.fr/Book-And-Report-Series/Iarc-Technical-Publications and www.uicc.org.

Principles of Essential TNM*

Essential TNM is a complement to TNM, to assign stage at diagnosis at cancer registries. It is for use by registrars when either the traditional (or full) TNM stage group (I, II, III or IV) or TNM staging components (T, N and M) have not been explicitly recorded in the patient's record.

Essential TNM follows a logical pathway documenting the furthest extent of disease in each cancer patient using combined clinical and/or operative/pathologic information available through the completion of surgery (if performed).

*Reference

Piñeros M, Parkin DM, Brierley J, eds. *User's Guide to Essential TNM* (IARC Technical Publications No. 48). Lyon, France: International Agency for Research on Cancer, 2024. Available from: https://publications.iarc.who.int/647. Licence: CC BY-NC-ND 3.0 IGO.

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

Rules for Classification

Essential TNM is composed of three key components that together summarise the extent of cancer in the patient at the time of diagnosis. The components are:
M: Presence or absence of distant metastasis
N: Presence or absence of regional lymph node metastasis/involvement
T: Extent of invasion and/or size of the tumour

Data extraction from medical records is facilitated through the use of flowcharts that include relevant questions and figures to help identify the extent of disease in different cancers. These flowcharts currently correspond to the eighth edition and when unchanged the ninth edition of the UICC TNM classification. They will be updated as required. The latest versions of the flowcharts are available in the User's Guideline at www.uicc.org and http://www.iacr.com.fr/.

The flowchart for staging breast cancer using Essential TNM is included as an example. Flowcharts exist as well for oesophageal carcinoma, colon and rectal carcinomas, hepatocellular carcinoma, cervical carcinoma, ovarian carcinoma, prostatic carcinoma and lymphoma.

Coding the Components of Essential TNM

Below is a simplified description of the concepts of coding. Full details and instructions are given in the Essential TNM User's Guide (www.iacr.com.fr).

The components of Essential TNM follow the full TNM eighth and ninth edition and are as follows:
Metastasis (M)

M+ Presence of distant metastasis, clinically or pathologically
M— No mention of distant metastases

Regional Node Metastasis/Involvement (N)

R+ Presence of regional node metastasis/involvement, clinically or pathologically
R2 Regional node metastasis is advanced
R1 Regional node metastasis is limited
R— No mention of regional node metastases
Record as R+ in the presence of documented regional node involvement, R— otherwise.

Extent of Invasion and/or Size of Tumour (T)

A Extent of invasion and/or tumour size is Advanced
A2 Extent of invasion and/or tumour size is very advanced
A1 Extent of invasion and/or tumour size is advanced
L Extent of invasion and/or tumour size is limited
L2 Extent of invasion and/or tumour size is limited
L1 Extent of invasion and/or tumour size is very limited
X Extent of invasion and/or tumour size cannot be assessed

In the absence of specific information on Metastases, Nodes, Tumour size/extent for M and N, if there is no information on their presence, it is assumed that they are absent (M–, R–). If regional nodes are mentioned but it cannot be distinguished between advanced or limited metastasis for regional nodes, R+ is coded.

In a similar manner, for T, if the degrees of tumour extension cannot be determined, T is coded as A or L (depending on the cancer site, see flowcharts).

For T, X is recorded if there is known to be a primary tumour, but there is no description of its size or extent.

Assigning the Essential TNM Stage Group

Once the Essential TNM component(s) have been coded, the components can be combined into Stage groups ranging from I to IV. These are comparable to TNM stage groups, designed to group cancer patients with similar prognosis.

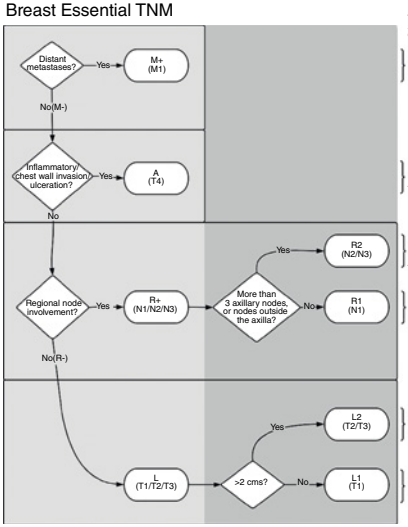
Essential TNM Example – Flowchart For Breast Cancer

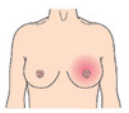
Breast Cancer Essential TNM

Key points for breast cancer staging

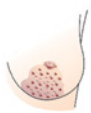
1. Metastasis is common to the bone, lungs and brain. Look for evidence on imaging.
2. Remember that lymph nodes on the opposite (i.e. contralateral) side or in the neck are distant metastases (M+).
3. If M+, Stage IV can be assigned and no need to look for further information.
4. Look for tumour extension to breast skin (epidermis).
5. Regional lymph nodes are axillary (includes intramammary), infraclavicular, internal mammary and supraclavicular on the same side as the tumour (see pictures in the flowchart).
6. If lymph node involvement (R+) has been established but no further information is available on number of nodes and location, assume R+. In such an event, the case will be allotted to the lower stage category (following Rule 4 of TNM), e.g., to Stage II Regional Limited.
7. Size of the tumour is a critical aspect and a tumour 2 cm or less is 'very limited' (Stage I).
8. If two malignant tumours are present in the same breast, use the one having the biggest size to stage.

Breast Essential TNM



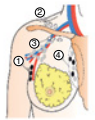


A(T4): Inflammatory carcinoma

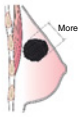


A(T4): Peau d'orange

A(T4): Ulceration/ Extension to chest wall



Regional lymph nodes:
1 Axillary
2 Supraclavicular
3 Intraclavicular
4 Internal mammary



L2 (T2/T3)

More than 2cm

L1 (T1)

2cm or less

Paediatric Tumours

Introductory Notes (see also page 14)

The classifications in this section are not intended to replace the classifications used by the clinician when treating an individual patient but to facilitate the collection of stage by population-based cancer registries. The consensus meetings held in 2014 and 2019 recommended a tiered staging system with more-detailed systems for well-resourced cancer registries (Tier 2) and less-detailed systems for registries with limited resources and access (Tier 1); as with Essential TNM, lower-tiered systems are based on collapsing higher-tiered systems.[1,2] The recommendations for tier 1 and 2 follow. Well-resourced registries may choose to collect additional accepted prognostic factors such as those used in the clinical setting, but these are not included in this section. For some cancers, recommendations are the same as described earlier for adult patients and the appropriate page number is given; others are referenced where appropriate. Rules for the derivation of paediatric cancer stage in population-based cancer registries are available from the UICC website.[3]

Rules for Classification

The classification applies only to paediatric malignant tumours.

Gastrointestinal Tumours

Hepatoblastoma

Tier 1 and 2

Localised	Tumour confined to the liver including regional lymph nodes
Metastatic	Distant metastases present

Well-resourced cancer registries may wish to add the PRETEXT[4] (PRE-Treatment EXTent of tumour) Group to Tier 2. The Pretext number describes the intrahepatic extent of the primary tumour before therapy (imaging based).

I	One section of the liver is involved and three adjoining sections* are free
II	One or two sections of the liver are involved and two adjoining sections are free; or caudate lobe only is involved

TNM Classification of Malignant Tumours, Ninth Edition. Edited by James Brierley, Meredith Giuliani, Brian O'Sullivan, Brian Rous, and Elizabeth Van Eycken.

III Two or three sections of the liver are involved and no two adjoining sections are free
IV All four sections of the liver are involved

Note
* Sections as defined by the PRETEXT classification.[4]

Bone and Soft Tissue Tumours

Osteosarcoma

Tier 1 and 2

Localised Tumour confined to the area of origin including regional lymph nodes
Metastatic Distant metastases present

Note
Skip lesions, skip metastases or seeding in the same bone as the primary tumour are considered localised and not metastatic. They are considered metastatic if located in a different bone than the primary tumour.

Ewing Sarcoma (bone or soft tissue)

Tier 1 and 2

Localised Tumour confined to the area of origin including regional lymph nodes
Metastatic Distant metastases present

Note
Skip lesions, skip metastases or seeding in the same bone as the primary tumour are considered localised and not metastatic. They are considered metastatic if located in a different bone than the primary tumour.

Rhabdomyosarcoma

Tier 1

Localised Tumour confined to the area of origin including regional lymph nodes
Metastatic Distant metastases present

Tier 2

A modified TNM classification with the addition of favourable or non-favourable tumour site is recommended.

T – Primary Tumour*

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour

T1 Tumour confined to a single anatomic site
  T1a Tumour 5 cm or less in greatest dimension
  T1b Tumour more than 5 cm in greatest dimension
T2 Extension beyond the anatomic site
  T2a Tumour 5 cm or less in greatest dimension
  T2b Tumour more than 5 cm in greatest dimension

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

pTNM Pathological Classification

The pT categories correspond to the clinical T categories**.**

Note

* For the TNM Classification, ninth edition in adults, see page 126.

Prognostic Grouping

The prognostic grouping for rhabdomyosarcoma includes favourable anatomical sites and unfavourable anatomical sites.

Favourable anatomical sites: Orbit, head and neck (scalp, parotid, oral cavity, larynx, oropharynx, cheek, hypopharynx, thyroid, parathyroid, neck but excluding parameningeal tumours), genitourinary sites (excluding bladder and prostate tumours), gallbladder and bile ducts

Unfavourable anatomic sites: Bladder, prostate, extremity, parameningeal (middle ear, nasal cavity, paranasal sinuses including tumours that extend into the paranasal sinus, nasopharynx, infratemporal fossa/pterygopalatine and parapharyngeal area), trunk, retroperitoneum and all other sites not noted as favourable

Stage I	Any T	Any N	M0	Favourable site
Stage II	T1a, T2a	N0	M0	Unfavourable site
Stage III	T1a, T2a	N1	M0	Unfavourable site
	T1b, T2b	Any N	M0	Unfavourable site
Stage IV	Any T	Any N	M1	Any site

Soft Tissue Sarcoma other than Rhabdomyosarcoma

Tier 1

Localised	Tumour confined to the area of origin including regional lymph nodes
Metastatic	Distant metastases present

Tier 2

The TNM classification is recommended as used for adults: See classification for soft tissue sarcoma of the extremity and superficial trunk on page 127.

Gynaecological Tumours

Ovary*

Tier 1

Localised	Tumour confined to the ovaries (one or both)
Regional	Tumour extension to pelvis, and/or peritoneum outside the pelvis, and/or retroperitoneal lymph nodes
Metastatic	Distant metastases excluding peritoneal metastases

Tier 2

A modified FIGO classification is recommended.

Stage I	Tumour confined to the ovaries (one or both)
Stage II	Tumour extension to pelvis without extension to peritoneum outside the pelvis nor to retroperitoneal lymph nodes
Stage III	Tumour extension to peritoneum outside the pelvis and/or retroperitoneal lymph nodes
Stage IV	Distant metastases present (excludes peritoneal metastases)

Alternatively, the TNM/FIGO Classification for ovarian tumours may be used, as for adults, see page 175.

Note

* Classification for germ cell tumours of the ovary. The UICC Stage corresponds to the FIGO stage.

Urological Tumours

Testis

Tier 1

Localised	Tumour confined to the testis
Regional	Tumour extension to regional lymph nodes (interaortocaval, para-aortic/periaortic, paracaval, preaortic, precaval, retroaortic, retrocaval, along spermatic cord)
Metastatic	Distant metastases present

Tier 2

The TNM classification is recommended as used for adults. See classification for testis on page 190.

Renal Tumours*

Tier 1

Localised	Tumour confined to the area of origin, including abdominal lymph nodes
Metastatic	Distant metastases present at diagnosis

Tier 2

Two Tier 2 classifications exist for Wilms Tumour. The classification of the Children's Oncology Group/National Wilms Tumour Study Group (COG/NWTSG) is utilised after surgical resection, prior to chemotherapy. The classification of the International Society of Paediatric Oncology (SIOP) is utilised if chemotherapy has been given preoperatively, prior to surgical resection.[5]

Note

* Excluding renal cell carcinoma.

COG/NWTSG

Based on findings at surgery for patients who *have not* received chemotherapy prior to surgery

pStage I Tumour is limited to the kidney and completely excised:

- Renal capsule intact, not penetrated by tumour
- No tumour invasion of veins or lymphatics of renal sinus
- No nodal or haematogenous metastases
- No prior biopsy
- Negative margins

pStage II Tumour extends beyond kidney but completely resected:

- Tumour penetrates renal capsule
- Tumour in lymphatics or veins of renal sinus
- Tumour in renal vein with margin not involved
- No nodal or haematogenous metastases
- Negative margins

pStage III Residual tumour or nonhaematogenous metastases confined to abdomen:

- Involved abdominal nodes
- Peritoneal contamination or tumour implant
- Tumour spillage of any degree occurring before or during surgery
- Gross residual tumour in abdomen
- Biopsy of tumour (including fine-needle aspiration) prior to removal of kidney
- Resection margins involved by tumour

Stage IV Haematogenous metastases or spread beyond abdomen *at diagnosis*

SIOP

Based on findings at surgery for patients who have received chemotherapy prior to surgery

ypStage I Tumour is limited to the kidney and completely resected:

- Renal capsule may be infiltrated by tumour, but tumour does not reach the outer surface
- Tumour may protrude or bulge into the pelvic system or ureter but does not infiltrate
- Vessels of renal sinus not involved

ypStage II Tumour extends beyond kidney but completely resected:

- Tumour penetrates renal capsule into perirenal fat
- Tumour infiltrates the renal sinus and/or invades blood and lymphatics vessels outside renal parenchyma but is completely resected
- Tumour infiltrates adjacent organs or vena cava but is completely resected

ypStage III Incomplete excision of the tumour (gross or microscopic extension beyond the resection margins):

- Involved abdominal lymph nodes, including necrotic tumour or chemotherapy-induced changes
- Tumour rupture before or intraoperatively
- Tumour has penetrated the peritoneal surface
- Tumour thrombi present at resection margins
- Surgical biopsy prior to resection (does not include needle biopsy)

Stage IV Haematogenous metastases or spread beyond abdomen *at diagnosis*

Ophthalmic Tumours

Retinoblastoma

Tier 1

Localised	Intraocular
Regional	Orbital extension or regional lymph nodes
Metastatic	Distant metastases present

Tier 2

The International Retinoblastoma Staging System (IRSS) is recommended.[6] This classification is determined after enucleation and is therefore a pathological classification.

Stage 0	The tumour is confined to the globe. Enucleation has not been performed
Stage I	Enucleation with negative margins
Stage II	Enucleation with microscopic residual disease
Stage III	Involvement of the orbit and/or metastases to regional lymph nodes
Stage IV	Distant metastatic disease

Note

Well-resourced cancer registries may wish to use the TNM classification page 217 as in adults.

Lymphoma

Hodgkin Lymphoma

Tier 1 and Tier 2

The Lugano classification (a modification of the Ann Arbor classification) is recommended as used for adults, see classification for Hodgkin Lymphoma on page 227.

Non-Hodgkin Lymphoma

Tier 1

Limited	No involvement of bone marrow and no involvement of CNS
Advanced	Involvement of bone marrow and/or CNS

Tier 2

The St Jude/Murphy system is recommended:[7]

Stage I	Involvement of a single tumour mass or nodal area, excluding the mediastinum and abdomen
Stage II	Involvement of a single tumour mass with regional node(s) or two or more tumours and/or nodal regions on the same side of the diaphragm, or a completely resected primary gastrointestinal tract tumour with or without regional nodal involvement

Stage III Tumour masses and/or regional nodes on opposite sides of the diaphragm or primary intrathoracic tumour (pulmonary, hilar, mediastinal, pleural or thymic) or extensive primary intra-abdominal disease or paraspinal tumour or epidural tumour

Stage IV Involvement of bone marrow and/or central nervous system

Leukaemia

Acute Lymphoblastic Leukaemia

Tier 1

CNS– No clinical signs* of central nervous system (CNS) involvement and no blasts in cerebrospinal fluid (CSF)

CNS+ Clinical signs* of CNS involvement or blasts in CSF

Tier 2

The Children's Oncology Group (COG) system is recommended, which is based on signs of central nervous system (CNS) involvement, the presence of blasts in cerebrospinal fluid (CSF) and the count of white blood cells (WBC) and red blood cells (RBC) in CSF and blood.[8]

CNS 1 No clinical signs* of CNS involvement and no blasts in CSF

CNS 2 No clinical signs* of CNS involvement and blasts in CSF with either (WBC < 5μL CSF) or (WBC ≥ 5μL CSF and RBC ≥ 10μL CSF and WBC/RBC in CSF ≤ 2x WBC/RBC in blood)

CNS 3 Clinical signs* of CNS involvement
or
blasts in CSF and WBC ≥ 5 μL CSF and either
(RBC < 10μL CSF) or (RBC ≥ 10μL CSF and WBC/RBC in CSF > 2x WBC/RBC in blood)

Note

* Clinical signs of CNS involvement includes radiologic evidence of intracranial, intradural mass; cranial nerve palsy; eye/brain involvement or hypothalamic syndrome. Extra-ocular orbital masses, severe headaches and eye swelling (in the absence of signs of cranial nerve involvement) are not sufficient to constitute CNS involvement.

Central Nervous System

Astrocytoma

Tier 1 and Tier 2

Localised	Localised disease
Metastatic	Distant metastasis

Medulloblastoma, Other Central Nervous System Embryonal Tumours and Ependymoma

Tier 1

Localised	Localised disease
Metastatic	Disease beyond local site (e.g., other lesions in brain or spine, tumour cells in CSF or distant metastases)

Tier 2

The Medulloblastoma staging system, a classification based on the extent of metastatic disease is recommended.[8,9]

- M0 Absence of visible disease beyond the primary tumour on imaging (MRI brain and spine) and absence of tumour cells in the cerebrospinal fluid
- M1 Tumour cells in the cerebrospinal fluid
- M2 Visible metastases in the brain
- M3 Visible metastases in the spine or cervicomedullary (junction)
- M4 Metastases outside of the central nervous system

Cancer registries may wish to specify the M-category, see page 225

Neuroblastoma

Tier 1

Localised	Localised not involving vital structures and confined to one body compartment, (neck, chest, abdomen or pelvis)
Locoregional	More extensive without metastatic disease
Metastatic	Distant metastatic disease except stage MS
MS	Metastatic disease confined to skin, liver and/or bone marrow in a patient less than 18 months of age

Tier 2

The stage classification of the International Neuroblastoma Risk Group Staging System (INRGSS) is recommended and is a clinical system determined prior to any treatment, including surgery.[10] It depends on the presence or absence of image-defined risk factors (IDRFs*), identified at diagnosis:

Stage L1 Localised tumour confined to one body compartment (neck, chest, abdomen or pelvis) and with the absence of IDRFs. An isolated finding of intraspinal tumour extension that does not fulfil the criteria for an IDRF is consistent with stage L1.

Stage L2 Locoregional tumour with the presence of one or more IRDFs. The tumour may be ipsilateral contiguous within body compartments (i.e., a left-sided abdominal tumour with left-sided chest involvement should be considered stage L2). However, a clearly left-sided abdominal tumour with right-sided chest (or vice versa) involvement is defined as metastatic disease.

Stage M Distant metastatic disease (i.e., not contiguous with the primary tumour) except as defined for stage MS. Non-regional (distant) lymph node involvement is metastatic disease. However, an upper abdominal tumour with enlarged lower mediastinal nodes or a pelvic tumour with inguinal lymph node involvement is considered locoregional disease. Ascites and/or pleural effusion, even with malignant cells, do not constitute metastatic disease unless they are remote from the body compartment of the primary tumour.

Stage MS Metastatic disease confined to skin, liver and/or bone marrow in children less than 18 months of age (547 days). MIBG scintigraphy must be negative in bone and bone marrow.

Notes

* IDRFs
- Ipsilateral tumour extension within two body compartments
  - Neck-chest, chest-abdomen, abdomen-pelvis
- Neck
  - Tumour encasing carotid and/or vertebral artery and/or internal jugular vein
  - Tumour extending to the base of skull
  - Tumour compressing the trachea
- Cervico-thoracic junction
  - Tumour encasing brachial plexus roots
  - Tumour encasing subclavian vessels and/or vertebral and/or carotid artery
  - Tumour compressing the trachea
- Thorax
  - Tumour encasing the aorta and/or major branches
  - Tumour compressing the trachea and/or principal bronchi
  - Lower mediastinal tumour, infiltrating the costo-vertebral junction between T9 and T12
- Thoraco-abdominal
  - Tumour encasing the aorta and/or vena cava

- Abdomen/pelvis
  - Tumour infiltrating the porta hepatis and/or the hepatoduodenal ligament
  - Tumour encasing branches of the superior mesenteric artery at the mesenteric root
  - Tumour encasing the origin of the coeliac axis and/or of the superior mesenteric artery
  - Tumour invading one or both renal pedicles
  - Tumour encasing the aorta and/or vena cava
  - Tumour encasing the iliac vessels
  - Pelvic tumour crossing the sciatic notch
- Intraspinal tumour extension whatever the location provided that:
  - More than one-third of the spinal canal in the axial plane is invaded and/or the perimedullary leptomeningeal spaces are not visible and/or the spinal cord signal is abnormal
- Infiltration of adjacent organs/structures
  - Pericardium, diaphragm, kidney, liver, duodeno-pancreatic block and mesentery

References

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