Lung Cancer
Histopathology Reporting Guide

Family/Last name

Given name(s)

Date of birth DD – MM – YYYY

Patient identifiers

Date of request DD – MM – YYYY

Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.
☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

OPERATIVE PROCEDURE (select all that apply)

- ☐ Wedge resection
- ☐ Segmentectomy
- ☐ Lobectomy
- ☐ Bilobectomy
- ☐ Pneumonectomy
- ☐ Sleeve resection
- ☐ Other, *specify*

SPECIMEN LATERALITY

- ◯ Left
- ◯ Right
- ◯ Not specified

ATTACHED ANATOMICAL STRUCTURES

- ◯ None submitted
- ◯ Submitted, *specify*

ACCOMPANYING SPECIMENS (select all that apply)

- ◯ None submitted
- ☐ Lymph node(s)
- ☐ Other, *specify*

TUMOUR SITE (select all that apply)

- ☐ Upper lobe
- ☐ Middle lobe
- ☐ Lower lobe
- ☐ Bronchus, *specify site(s)*

MULTIPLE TUMOUR NODULES (Note 1)

- ◯ Cannot be assessed
- ◯ Absent
- ◯ Present
  - ◯ Synchronous primary[a]
  - ◯ Intra pulmonary metastasis
    - Number of tumours
    - Site (select all that apply)
      - ☐ Same lobe
      - ☐ Different ipsilateral lobe
      - ☐ Contralateral lung
  - ◯ Indeterminate
    - Further evaluation pending
      - ◯ Yes ◯ No

[a] *Core elements should be reported for each synchronous primary tumour.*

MACROSCOPIC APPEARANCE OF PLEURA OVERLYING TUMOUR (Note 2)

Specify

ATELECTASIS/OBSTRUCTIVE PNEUMONITIS EXTENDING TO HILAR REGION (Note 3)

- ◯ Not assessable
- ◯ Absent
- ◯ Present

TUMOUR DIMENSION (Note 4)

- ◯ Cannot be determined

Maximum invasive size *(Applicable to resected non-mucinous adenocarcinoma)* mm

AND/OR

Total tumour size mm

TUMOUR INVOLVES MAIN BRONCHUS

- ◯ Not applicable
- ◯ Cannot be assessed
- ◯ Not identified
- ◯ Present

BLOCK IDENTIFICATION (Note 5)

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

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HISTOLOGICAL TUMOUR TYPE (Note 6) (select all that apply)
(Value list based on the World Health Organization, Classification of Thoracic Tumours (2021))

- ☐ Adenocarcinoma
  - Classification of Adenocarcinoma
    - ☐ Adenocarcinoma in situ (AIS)
      - ◯ Non-mucinous ◯ Mucinous
    - ☐ Minimally invasive adenocarcinoma (MIA)
      - ☐ Non-mucinous ☐ Mucinous
    - ☐ Invasive non-mucinous adenocarcinoma
      - PREDOMINANT SUBTYPE
        - ◯ Lepidic ◯ Micropapillary
        - ◯ Acinar ◯ Solid
        - ◯ Papillary ◯ Other, *specify*
      - SUBTYPE PERCENTAGES
        - Lepidic → %
        - Acinar → %
        - Papillary → %
        - Micropapillary → %
        - Solid → %
      - OTHER PATTERNS (e.g., cribriform and/or fused glands), *if present*
        - TYPE OF PATTERN → %
        - TYPE OF PATTERN → %
        - TYPE OF PATTERN → %
    - ☐ Invasive mucinous adenocarcinoma
      - ◯ Mixed invasive mucinous and non-mucinous adenocarcinoma
    - ☐ Colloid adenocarcinoma
    - ☐ Fetal adenocarcinoma
    - ☐ Enteric-type adenocarcinoma
- ☐ Squamous cell carcinoma
  - ◯ Squamous cell carcinoma, NOS
    - ◯ Squamous cell carcinoma, keratinizing
    - ◯ Squamous cell carcinoma, non-keratinizing
    - ◯ Basaloid squamous cell carcinoma
  - ◯ Lymphoepithelial carcinoma
- ☐ Neuroendocrine carcinomas
  - ◯ Small cell carcinoma
  - ◯ Large cell neuroendocrine carcinoma
- ☐ Neuroendocrine tumours
  - ◯ Typical carcinoid
  - ◯ Atypical carcinoid
- ☐ Large cell carcinoma
- ☐ Other, *specify*

DISTANCE OF TUMOUR TO CLOSEST RESECTION MARGIN (Note 7)

mm

◯ Cannot be assessed

HISTOLOGICAL TUMOUR GRADE (Note 8)
(Applicable to resected invasive non-mucinous adenocarcinoma)

◯ Grade 1
◯ Grade 2
◯ Grade 3

RESPONSE TO NEOADJUVANT THERAPY (Note 9)

◯ Prior neoadjuvant therapy not known
◯ No prior neoadjuvant therapy
◯ Known neoadjuvant therapy

Viable tumour as a % of tumour bed %

Major pathological response (<10% viable tumour)
◯ Absent ◯ Present

Complete pathological response (no residual viable tumour)
◯ Absent ◯ Present

Necrosis
◯ Not identified
◯ Present
Extent of necrosis %

Stroma (including fibrosis)
◯ Not identified
◯ Present
Extent of stroma %

Inflammation
◯ Mild
◯ Moderate
◯ Severe

DIRECT INVASION OF ADJACENT STRUCTURES (Note 10)
(select all that apply)

◯ Not applicable
◯ Not identified
☐ Chest wall
☐ Phrenic nerve
☐ Parietal pericardium
☐ Diaphragm
☐ Mediastinum
☐ Mediastinal fat
☐ Mediastinal pleura
☐ Great vessels
☐ Trachea
☐ Recurrent laryngeal nerve
☐ Oesophagus
☐ Vertebral body
☐ Heart

LYMPHOVASCULAR INVASION (Note 11)

◯ Indeterminate
◯ Not identified
◯ Present

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VISCERAL PLEURAL INVASION (Note 12)

- ◯ Cannot be assessed
- ◯ Indeterminate
- ◯ Not identified
- ◯ Present

Extent of pleural involvement

◯ PL1 ◯ PL2 ◯ PL3

SPREAD THROUGH AIR SPACES (STAS) (Note 13)

- ◯ Indeterminate
- ◯ Not identified
- ◯ Present

PERINEURAL INVASION

- ◯ Indeterminate
- ◯ Not identified
- ◯ Present

OTHER NEOPLASTIC PROCESSES AND PRECURSORS

Specify (e.g., tumourlets, dysplasia, neuroendocrine cell hyperplasia (NEH), atypical adenomatous hyperplasia (AAH))

NON-NEOPLASTIC LUNG DISEASE

Specify

SURGICAL MARGIN STATUS (Note 14)

Bronchial margin

- ◯ Not applicable
- ◯ Not involved
- ◯ Involved by invasive carcinoma
- ◯ Involved by carcinoma in situ only
- ◯ Only peribronchial soft tissue involved

Vascular margin

- ◯ Not applicable
- ◯ Not involved
- ◯ Involved
- ◯ Only perivascular soft tissue involved

Other margin 1 (e.g., parenchymal, chest wall margin or sleeve resection proximal and distal margins), *specify*

- ◯ Not applicable
- ◯ Not involved
- ◯ Involved

Other margin 2 (e.g., parenchymal, chest wall margin or sleeve resection proximal and distal margins), *specify*

- ◯ Not applicable
- ◯ Not involved
- ◯ Involved

Residual tumour status (R)

- ◯ R0 - No residual tumour
- ◯ R0 (un) - Residual tumour status not known
- ◯ R1 - Microscopic residual tumour
- ◯ R2 - Macroscopic residual tumour

LYMPH NODE STATUS (Note 15)

Station(s) examined, *specify*

- ◯ Cannot be assessed
- ◯ Not involved
- ◯ Involved by micrometastasis only
- ◯ Involved

Stations involved, *specify*

Total number of lymph nodes examined

Total number of involved lymph nodes

◯ Number cannot be determined

Involved station 1, *specify*

Total number of lymph nodes from this site

Number of involved lymph nodes

◯ Number cannot be determined

Involved station 2, *specify*

Total number of lymph nodes from this site

Number of involved lymph nodes

◯ Number cannot be determined

Involved station 3, *specify*

Total number of lymph nodes from this site

Number of involved lymph nodes

◯ Number cannot be determined

Extracapsular extension

- ◯ Cannot be determined
- ◯ Not identified
- ◯ Present, *specify station*

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ANCILLARY STUDIES

Immunohistochemical markers (Note 16)

- ◯ Not performed
- ◯ Performed

Positive antibodies	
Negative antibodies	
Equivocal antibodies	

Conclusions

Molecular data (Note 17)

- ◯ Not performed
- ◯ Pending
- ◯ Performed

EGFR result
- ◯ Indeterminate
- ◯ Mutation absent
- ◯ Mutation present, *describe*

ALK result
- ◯ Indeterminate
- ◯ Rearrangement absent
- ◯ Rearrangement present, *describe*

ROS1 result
- ◯ Indeterminate
- ◯ Rearrangement absent
- ◯ Rearrangement present, *describe*

RET result
- ◯ Indeterminate
- ◯ Rearrangement absent
- ◯ Rearrangement present, *describe*

NTRK result
- ◯ Indeterminate
- ◯ Rearrangement absent
- ◯ Rearrangement present, *describe*

BRAF result
- ◯ Indeterminate
- ◯ Mutation absent
- ◯ Mutation present, *describe*

KRAS result
- ◯ Indeterminate
- ◯ Mutation absent
- ◯ Mutation present, *describe*

MET result
- ◯ Indeterminate
- ◯ Variant not identified
- ◯ Variant present, *specify*

HER2 result
- ◯ Indeterminate
- ◯ Variant not identified
- ◯ Variant present, *specify*

Immuno-oncological data

PDL1 result
- ◯ Indeterminate

Percentage tumour cells positive %

Antibody clone used

Other, *record test(s), methodology and results*

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

HISTOLOGICALLY CONFIRMED DISTANT METASTASES (Note 18)

- ◯ Cannot be assessed
- ◯ Not identified
- ◯ Present, *specify site(s)*

PATHOLOGICAL STAGING (UICC TNM 8th edition)[b] (Note 19)

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

- ☐ m - multiple primary tumours at a single site
- ☐ r - recurrent tumours after a disease free period
- ☐ y - classification is performed during or following multimodality treatment

Primary tumour (pT)

- ◯ TX[c] 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
- ◯ T0 No evidence of primary tumour
  - ◯ Tis Carcinoma in situ[d]
- ◯ T1 Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus (i.e., not in the main bronchus)[e]
  - ◯ T1mi Minimally invasive adenocarcinoma[f]
  - ◯ T1a Tumour 1 cm or less in greatest dimension[e]
  - ◯ T1b Tumour more than 1 cm but not more than 2 cm in greatest dimension[e]
  - ◯ T1c Tumour more than 2 cm but not more than 3 cm in greatest dimension[e]
- ◯ T2 Tumour more than 3 cm but not more than 5 cm; or tumour with any of the following features:[g]
  - Involves main bronchus regardless of distance to the carina, but without involvement of the carina
  - Invades visceral pleura
  - Associated with atelectasis or obstructive pneumonitis that extends to the hilar region either involving part of or the entire lung
  - ◯ T2a Tumour more than 3 cm but not more than 4 cm in greatest dimension
  - ◯ T2b Tumour more than 4 cm but not more than 5 cm in greatest dimension
- ◯ T3 Tumour more than 5 cm but not more than 7 cm in greatest dimension or one that directly invades any of the following: parietal pleura, chest wall (including superior sulcus tumours) phrenic nerve, parietal pericardium; or separate tumour nodule(s) in the same lobe as the primary
- ◯ T4 Tumour more than 7 cm or of any size that invades any of the following: diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina; separate tumour nodule(s) in a different ipsilateral lobe to that of the primary

Regional lymph nodes (pN)

- ◯ NX[c] Regional lymph nodes cannot be assessed
- ◯ N0 No regional lymph node metastasis
- ◯ N1 Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
- ◯ N2 Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
- ◯ N3 Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

[b] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley (incorporating any errata published up until 25th January 2022).*

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

[d] *Tis includes adenocarcinoma in situ and squamous carcinoma in situ.*

[e] *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.*

[f] *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.*

[g] *T2 tumours with these features are classified T2a if 4 cm or less, or if size cannot be determined and T2b if greater than 4 cm but not larger than 5 cm.*

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a core element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

Non-morphological testing e.g., molecular or immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) recommends that some ancillary testing in ICCR Datasets is included as core elements. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

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Scope

The dataset has been developed for the pathology reporting of resection specimens of malignant epithelial cancers of the lung. The dataset applies to small cell carcinoma and carcinoid tumours, as well as non-small cell types of lung carcinoma. While originally used primarily for non-small cell lung carcinoma, the TNM staging system[2,3] has since also been validated for small cell carcinoma and carcinoid tumours.[4]

Benign tumours may be reported at the discretion of the pathologist though not all core elements will be applicable, e.g., TNM staging. It is not applicable for bronchoscopic and transthoracic biopsy specimens. Synchronous primary tumours should be reported separately, denoting each staging with a suffix of 'm' so that multiplicity is documented. Data from non-epithelial tumours should be collected using other ICCR datasets,[5] where available (e.g., primary pulmonary lymphomas, sarcomas).

The fourth edition includes changes to align the dataset with the 2021 World Health Organization (WHO) Classification of Thoracic Tumours, 5th edition.[6]

The authors of this dataset can be accessed here.

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Note 1 – Multiple tumour nodules (Core)

Occasionally, more than one discrete tumour nodule is identified in lung cancer resection specimens. It is important to distinguish synchronous primary tumours from a tumour displaying intrapulmonary metastases, as they have different prognoses and are staged differently.[2,3] Tumours can be considered a second primary if they are different histological types (e.g., squamous cell carcinoma and adenocarcinoma) or are clearly different by comprehensive histological assessment (proportion of different patterns, grade, cytologic and stromal features),[7] or if they are a squamous cell carcinoma that has arisen from carcinoma in situ (CIS).[8] It is more challenging if the histological appearances of both tumours are similar. Features that may assist in determining a tumour as an intrapulmonary metastasis include similar features by comprehensive histological assessment, identical driver mutations or significant nodal or systemic metastases.[8] Generally, multiple lepidic or lepidic predominant non-mucinous adenocarcinomas (ground-glass or part-solid nodules radiologically) are considered separate primary tumours.[8] In some cases, multidisciplinary team discussion may be required for final determination. If there remains doubt, then the lower stage option should be provided.

Synchronous primary tumours should be recorded as such in the pathology report with the highest T category followed by the suffix 'm', indicating multiplicity, or the number of tumours in parentheses (e.g., T1b(m) or T1b(2)).

Patients with intrapulmonary metastases in the same lobe have survival outcomes similar to patients with solitary tumours that by size or other criteria fall into the T3 category and for this reason are staged similarly. Analogously, the similarity in survival between patients with multiple tumour nodules considered to be intrapulmonary metastases as in different lobes of the same lung and patients with solitary tumours that fulfil T4 criteria, has led the Union for International Cancer Control (UICC)[2] and American Joint Committee on Cancer (AJCC)[3] to recommend staging such patients similarly.

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Note 2 – Macroscopic appearance of pleura overlying tumour (Non-core)

The macroscopic appearance of the visceral pleural overlying a tumour can help to guide the submission of tissue blocks and gauge the index of suspicion for visceral pleural invasion (VPI). Areas of pleural puckering or distortion directly overlying a tumour should be sampled to enable assessment for possible pleural invasion. It is important to note, however, that macroscopic visceral pleural puckering is not itself diagnostic of VPI.[9] The presence of VPI must be confirmed histologically.

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Note 3 – Atelectasis/obstructive pneumonitis extending to hilar region (Core)

The presence and extent of atelectasis/obstructive pneumonia factor should be assessed as part of assigning a T category. While most likely to be seen in association with central tumours that obstruct either the main or proximal lobar bronchi, this staging parameter can be difficult to accurately assess in resected specimens and often requires correlation with the radiological findings.[10] In certain instances, the lack of availability of radiologic information renders this parameter not assessable. In the 8th edition of the UICC[2] and AJCC[3] Staging Systems, the staging impact of atelectasis/obstructive pneumonitis has been modified from the 7th edition. According to the 8th edition, unless other features dictate a higher T category, atelectasis or obstructive pneumonitis that extends to the hilar region, involving part or all of the lung, is categorised as pT2.

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Note 4 – Tumour dimension (Core)

Tumour size has long been recognised as an important prognostic indicator in lung cancer.[11] For non-mucinous lung adenocarcinoma, the invasive size (excluding any lepidic component) should be recorded as this is now used for the T descriptor in staging of lung cancer.[12] This is a feature of the 8th edition of the TNM staging classification following recommendations from the UICC[2] and AJCC[3] and based on increasing data that invasive size is a better predictor of survival than total tumour size, especially in tumours ≤30 millimetres (mm).[12] By contrast, invasive mucinous adenocarcinomas are staged according to their total tumour size, even if they are extensively lepidic. In cases of non-mucinous adenocarcinoma where invasive foci are multifocal, the proportion of invasive components can be used to estimate the size of the invasive component (i.e., if 50% of a non-mucinous adenocarcinoma with maximum total size of 28 mm comprises non-lepidic patterns, then the invasive size would be estimated as 14 mm).

The total tumour size, usually measured macroscopically, should also be included. In problematic cases, review of the measurements on computerised tomography of total size and solid components may be of value.[13] In specimens harbouring multiple synchronous primaries, assignment of the T category is based on the invasive size of the largest tumour.

Care should be taken not to overestimate tumour size by including areas of adjacent obstructive pneumonia in the tumour measurement. The gross assessment of tumour size should be confirmed microscopically and in cases where adjacent obstructive pneumonia has been mistakenly incorporated into the tumour measurement, tumour size should be adjusted accordingly.

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Note 5 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded, including the optimal block for any future ancillary studies, such as molecular analysis, and any blocks taken for research. This information should ideally be documented in the final pathology report and particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be

available on the laboratory computer system and relayed to the reviewing pathologist. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials.

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Note 6 – Histological tumour type (Core and Non-core)

All lung carcinomas should be classified according to the most recent edition of the WHO Classification of Tumours of the Lung, 5th edition, 2021 (Table 1).[6] Accurate typing of lung carcinoma is important, as histology impacts on decisions to proceed with molecular testing (see below) and the most appropriate treatment regimen for patients in whom adjuvant therapy is indicated or for patients who relapse with advanced stage disease. Given the essential role that histologic type plays in patient management, a designation of non-small cell lung carcinoma, not otherwise specified (NSCLC, NOS), is not acceptable in resection specimens.[14] While it is beyond the scope of this document to provide a detailed discussion of the pathologic features of various histologic types of lung carcinoma, in undifferentiated cases, immunohistochemistry (IHC) (or a mucin stain for solid pattern adenocarcinoma) can greatly aid in classification and is required if available, for the diagnosis of non-keratinising squamous cell carcinoma, or solid pattern adenocarcinoma.

Lung carcinomas should be adequately sampled in order to ensure defining features are satisfactorily represented in the sections examined histologically. For cases in which adenocarcinoma in situ (AIS) or minimally invasive adenocarcinoma (MIA) are being considered, the International Association for the Study of Lung Cancer (IASLC), American Thoracic Society (ATS) and European Respiratory Society (ERS) recommend that lesions be entirely submitted for histopathologic examination.[6]

Table 1: World Health Organization classification of tumours of the lung.[6 a]

Descriptor	ICD-O codes[b]
Epithelial tumours	
Papillomas	
Squamous cell papilloma, NOS	8052/0
Squamous cell papilloma, inverted	8053/0
Glandular papilloma	8260/0
Mixed squamous cell and glandular papilloma	8560/0
Adenomas	
Sclerosing pneumocytoma	8832/0
Alveolar adenoma	8251/0
Papillary adenoma	8260/0
Bronchiolar adenoma/ciliated muconodular papillary tumour†	8140/0
Mucinous cystadenoma	8470/0
Mucous gland adenoma	8480/0
Precursor glandular lesions	
Atypical adenomatous hyperplasia	8250/0

Descriptor	ICD-O codes[b]
Adenocarcinoma in situ	
Adenocarcinoma in situ, non-mucinous	8250/2
Adenocarcinoma in situ, mucinous	8253/2
Adenocarcinomas	
Minimally invasive adenocarcinoma	
Minimally invasive adenocarcinoma, non-mucinous	8256/3
Minimally invasive adenocarcinoma, mucinous	8257/3
Invasive non-mucinous adenocarcinoma	
Lepidic adenocarcinoma	8250/3
Acinar adenocarcinoma	8551/3
Papillary adenocarcinoma	8260/3
Micropapillary adenocarcinoma	8265/3
Solid adenocarcinoma	8230/3
Invasive mucinous adenocarcinoma	8253/3
Mixed invasive mucinous and non-mucinous adenocarcinoma	8254/3
Colloid adenocarcinoma	8480/3
Fetal adenocarcinoma	8333/3
Adenocarcinoma, enteric-type	8144/3
Adenocarcinoma, NOS	8140/3
Squamous precursor lesions	
Squamous cell carcinoma in situ	8070/2
Mild squamous dysplasia	8077/0
Moderate squamous dysplasia	8077/2
Severe squamous dysplasia	8077/2
Squamous cell carcinomas	
Squamous cell carcinoma, NOS	8070/3
Squamous cell carcinoma, keratinizing	8071/3
Squamous cell carcinoma, non-keratinizing	8072/3
Basaloid squamous cell carcinoma	8083/3
Lymphoepithelial carcinoma	8082/3
Large cell carcinomas	
Large cell carcinoma	8012/3
Adenosquamous carcinomas	
Adenosquamous carcinoma	8560/3
Sarcomatoid carcinomas	
Pleomorphic carcinoma	8022/3
Giant cell carcinoma	8031/3
Spindle cell carcinoma	8032/3
Pulmonary blastoma	8972/3
Carcinosarcoma	8980/3
Other epithelial tumours	
NUT carcinoma	8023/3

Descriptor	ICD-O codes[b]
Thoracic SMARCA4-deficient undifferentiated tumour†	8044/3
Salivary gland–type tumours	
Pleomorphic adenoma	8940/0
Adenoid cystic carcinoma	8200/3
Epithelial-myoepithelial carcinoma	8562/3
Mucoepidermoid carcinoma	8430/3
Hyalinizing clear cell carcinoma†	8310/3
Myoepithelioma	8982/0
Myoepithelial carcinoma	8982/3
Lung neuroendocrine neoplasms	
Precursor lesion	
Diffuse idiopathic neuroendocrine cell hyperplasia	8040/0
Neuroendocrine tumours	
Carcinoid tumour, NOS/neuroendocrine tumour, NOS	8240/3
Typical carcinoid/neuroendocrine tumour, grade 1	8240/3
Atypical carcinoid/neuroendocrine tumour, grade 2	8249/3
Neuroendocrine carcinomas	
Small cell carcinoma	8041/3
Combined small cell carcinoma	8045/3
Large cell neuroendocrine carcinoma	8013/3
Combined large cell neuroendocrine carcinoma	8013/3

[a] This dataset is intended for the pathology reporting of malignant epithelial tumours. Benign tumours are listed in grey in Table 1 but use of this dataset for benign tumours would be at the discretion of the pathologist. Not all core elements will be applicable in the setting of benign tumours, e.g., TNM staging.
[b] These morphology codes are from the International Classification of Diseases for Oncology, third edition, second revision (ICD-O-3.2).[15] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; /3 for malignant tumours, primary site; and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries. This classification is modified from the previous WHO classification, taking into account changes in the understanding of these lesions. Subtype labels are indented.
† Labels marked with a dagger constitute a change in terminology of a previous code.

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Note 7 – Distance of tumour to closest resection margin (Core)

Although NHMRC level III-2 and above evidence[1] supporting inclusion of distance of tumour to the closest resection margin as a core element is not available, this information is necessary to facilitate post-operative treatment planning. Documentation of the macroscopic distance between a tumour and the nearest resection margin and specifying the closest margin is invaluable in cases where the distance is greater than that which could be encompassed in a tissue block. For cases in which the distance can be visualised on a microscopic slide, it is recommended that the macroscopic measurement be confirmed histologically.

The types of margins will vary according to the specimen received. For wedge resections, the only resection margin is the parenchymal margin, which is represented by the staple line. Larger resections may include parenchymal margins (e.g., lobectomies from patients with incomplete fissures) in addition to bronchial and vascular margins.

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Note 8 – Histological tumour grade (Core)

Invasive non-mucinous adenocarcinomas should be graded according to the IASLC grading system.[16] Lepidic predominant tumours are grade 1 and acinar or papillary predominant tumours grade 2, both with no or less than 20% of high grade patterns. Any tumour with at least 20% high grade patterns (solid, micropapillary, or complex glandular structures) is grade 3.

There are insufficient data to determine how to grade mucinous adenocarcinomas, squamous and adenosquamous carcinoma and as such, these tumours can be assigned the 'not applicable' category.[6]

According to the latest WHO Classification,[6] sarcomatoid carcinomas (pleomorphic carcinoma, carcinosarcoma) and pulmonary blastoma are classified as high grade (poorly differentiated) and large cell carcinoma is classified as undifferentiated.

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Note 9 – Response to neoadjuvant therapy (Core and Non-core)

Quantification of the extent of tumour regression in patients who have received neoadjuvant chemotherapy and/or radiation therapy is prognostically useful.[17,18] Histological response to neoadjuvant therapy must be recorded. Multidisciplinary guidelines for assessing pathological response to neoadjuvant therapy in lung cancer resections recommend histological assessment of the percentages of viable tumour, necrosis, and stroma (including fibrosis and inflammation), the total for which should add up to 100%. Inflammation should also be scored as mild, moderate or severe.[19] Major pathological response is defined as tumours with ≤10% viable tumour and pathological complete response (pCR) as no viable tumour. The 'y' prefix must be included as part of the TNM pathologic stage for patients that have received neoadjuvant therapy prior to resection. A study by Qu et al (2019) suggests that the optimal cut-off may be different for adenocarcinoma (65%) compared to squamous cell carcinoma (10%), so data should be collected as 10% increments.[20]

Assessment for major pathological response is undertaken on resected primary tumours while assessment for complete pathological response is based on evaluation of the primary tumour and any resected regional nodes. pCR is defined as lack of any viable tumour cells on review of hematoxylin and eosin stain (H&E) slides after complete assessment of a resected lung cancer specimen including all sampled regional lymph nodes. These tumours would be staged as ypT0N0 using the 8th edition UICC[2] and AJCC[3] Staging Systems.[19]

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Note 10 – Direct invasion of adjacent structures (Core)

Extension of tumour into extrapulmonary structures is an adverse prognostic factor, the degree of which depends on the structures involved.[2,3] Occasionally, lung cancer resections will include extrapulmonary structures either en bloc or separately. The presence or absence of invasion into extrapulmonary structures in such cases should be reported and the involved structures should be specified.

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Note 11 – Lymphovascular invasion (Core)

Lymphovascular invasion has been demonstrated to be an independent prognostic factor in lung carcinoma and is an exclusionary criterion for the new entities of AIS and MIA.[6,21-25] A number of studies have evaluated the prognostic impact of large vessel (arterial and/or venous) invasion independent of lymphatic invasion with somewhat conflicting results.[26-28] For this reason, it is permissible to report the presence of vascular and/or lymphatic invasion under the single heading of lymphovascular invasion.

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Note 12 – Visceral pleural invasion (Core)

The presence of tumour at the surface of the visceral pleura has been recognised as an independent adverse prognostic factor for quite some time.[11] More recently, penetration through the visceral pleural elastic layer was shown to have the same prognostic impact.[29,30] With the release of the current staging classification, criteria for visceral pleural invasion (VPI) have been more clearly defined to encompass both invasion beyond the visceral pleural elastic layer and extension to the visceral pleural surface.[9] For tumours that are in contact with the visceral pleura and do not clearly extend to the visceral pleural surface, elastic stains can aid in the detection of tumour cells beyond the visceral pleural elastic layer.

Sometimes, there are two perceptible visceral pleural elastic layers. In most individuals, the elastic layer that is closer to the surface of the visceral pleura, typically referred to as the outer or external elastic layer, is thicker and more continuous, while within the visceral pleural connective tissue adjacent to the alveolar parenchyma lies a less prominent and/or somewhat fragmented internal (inner) elastic layer. Although there has been debate over whether the thickest or the outermost layer should be used to distinguish PL0 from PL1, the expert consensus is to use the outermost elastic layer.[31] Occasionally, tumour cells are intermingled with fibres of the visceral pleural elastic layer without unequivocally penetrating beyond the visceral pleural elastic layer. This should not be interpreted as evidence of VPI.

A small percentage of cases are indeterminate for VPI. Occasionally, the visceral pleural elastic layer is imperceptible, even on elastic stains, in cases where tumour is in contact with the visceral pleura but does not extend to the visceral pleural surface. In such circumstances, the TNM classification dictates that the lower category be assigned (i.e., tumours should not be upstaged on the basis of equivocal VPI).[3] So too is the case when the visceral pleura in the vicinity of a tumour is fibrotic or elastotic to the point of obscuring the normal visceral pleural elastic landmarks so that elastin stains are difficult if not impossible to interpret. Rarely, due to adhesions or other technical factors, a specimen is received devoid of visceral pleura overlying a tumour and it is simply not possible to assess VPI.

Data on tumours that otherwise meet criteria for T1 that cross an interlobar fissure into an adjacent ipsilateral lobe but are not present on the visceral pleural surface are limited, but under current staging recommendations, are upcategorised as T2.[9]

The extent of pleural involvement must be recorded as it has prognostic significance and is used for pathological staging. The UICC[2] and AJCC[3] recommend the following staging scheme:[9]

PL0 - no penetration beyond the visceral pleural elastic layer

PL1 - tumour penetration beyond the visceral pleural elastic layer

PL2 - tumour extension to the visceral pleural surface, and

PL3 - extension into the parietal pleura.

PL0 is categorised as VPI absent, while both PL1 and PL2 types of VPI change the category of otherwise T1 tumours to T2. Tumours that would otherwise be categorised as T1 or T2 are changed to T3 if there is any parietal pleura invasion (PL3).[2,3,9] Assessment for PL3 can be difficult in the presence of adhesions between visceral and parietal pleura. No survival data are available based on the extent of parietal pleural invasion.

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Note 13 – Spread through air spaces (STAS) (Core)

The 2015 WHO Classification for Lung Cancer,[25] introduced the concept of spread through air spaces (STAS) as a new pattern of invasion in lung adenocarcinoma. STAS is defined as tumour cells within continuous alveolar spaces beyond the edge of the main tumour, often forming micropapillary clusters, and must be distinguished from artefactual spread of tumour cells.[6] The presence of STAS is associated with worse prognosis,[32,33] and increased risk of tumour recurrence in sublobar resections.[32] The extent of STAS is not included when measuring the invasive size of the tumour as it is considered a manifestation of tumour spread.[6]

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Note 14 – Surgical margin status (Core and Non-core)

Completeness of resection is not only an important prognostic factor, but also influences post-operative management, including decisions about adjuvant therapy.[34] The status of the surgical resection margin(s) should be reported for all resections, but the number and types of margins varies according to the specimen received. For wedge resections, the only resection margin is the parenchymal margin, which is represented by the staple line. One approach would be to cut beneath the staple line and assess the margin microscopically. If there is no involvement beneath the staple line, then the margin is considered not involved. If involved, then further examination of tissue within the staple line may be warranted, in conjunction with a discussion with the surgeon. The same principle can be applied to bronchial and vascular margins, with the option of dissecting out tissue from the staple line, or shaving from the proximal end if visible, should the cut immediately below the staple line(s) be positive.

Larger resections may include parenchymal margins (e.g., lobectomies from patients with incomplete fissures), in addition to bronchial and vascular margins. Depending on the anatomy and extent of resection, these may be singular (one bronchial margin and one vascular margin composed of an arterial and venous margin) or multiple.

A positive bronchial or vascular margin is widely considered to represent tumour within the lumen that is densely adherent to and/or involving the wall. According to several studies, tumour restricted to the peribronchial or perivascular soft tissue at the margin or the presence of lymphatic permeation alone at the margin is also prognostically important.[35-38] Recently, however, the significance of peribronchial soft tissue involvement without mucosal involvement has been called into question.[39] Data on the impact of intraluminal tumour alone at the margin are too limited to draw meaningful conclusions. When reporting the presence of tumour at the bronchial or vascular margin, the pathologist should delineate the nature of the involvement.

The significance of squamous CIS at the bronchial margin remains unresolved due to its rare occurrence.[40] Results of several studies suggest the presence of CIS at the margin is not an independent prognostic factor.[40,41] Nevertheless, it is important to report CIS at the margin so that additional data might permit a more conclusive assessment of its role in prognosis.

En bloc resections contain additional margins (e.g., rib, chest wall soft tissue), the nature of which is dependent on the type and extent of extrapulmonary structures resected. Ideally, the surgeon will designate the location of the resection margin(s) of extrapulmonary structures prior to submission of the specimen, but in ambiguous cases, direct communication will help to ensure appropriate handling and submission of tissue for histopathologic examination. The status of additional margin(s) and their location(s) should be specified in the pathology report.

R status may be recorded as:

R0 - complete resection
R1 - incomplete microscopic resection
R2 - incomplete macroscopic resection.

A value of R0(un) is used where there is any one of the following: <3 N1 and/or <3 N2 nodal stations sampled (always including subcarinal), highest mediastinal node removed is involved, CIS at the bronchial margin, or positive pleural lavage.[42,43]

R1 includes microscopic tumour at any one or more of the following: bronchial margin, vascular margin, soft tissue/mediastinal margin, tumour at soft tissue margin of a lymph node with extracapsular spread. Discussion with the surgeon in relation to surgical margins is recommended before assigning R1 status.

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Note 15 – Lymph node status (Core and Non-core)

Lymph node metastases are an adverse prognostic factor, the extent of which is dependent on the location of the involved lymph nodes.[44] The site(s) of involvement (lymph node stations) should be recorded according to the IASLC lymph node map.[3] Lymph nodes involved by metastatic tumour or direct invasion of tumour into N1 nodes are both considered positive nodes for the purposes of staging. Given the nature of the procedure, lymph nodes obtained by mediastinoscopy are often received fragmented and unless specified by the surgeon, it may not be possible to distinguish a single fragmented lymph node from fragments of multiple lymph nodes. For this reason, only if the actual number of nodes is known or provided should quantification be considered. Otherwise, only the involvement by, or absence of tumours in lymph node stations should be recorded without specifying the number involved. Cases with only micrometastasis (greater than 0.2 mm but less than or equal to 2 mm) to lymph nodes can be subclassified as involved by micrometastasis only. Isolated tumour cells (ITC) in lymph nodes (less than 0.2 mm in greatest dimension) do not impact the pN designation and cases with only ITC are classified as pN0(i+).[45] Direct invasion (and not

just metastatic spread) into an N1 lymph node is also classified as N1. Extracapsular extension to the margin of a nodal station specimen should also be documented as R1.

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Note 16 – Immunohistochemical markers (Core)

Immunohistochemical markers must be used for the diagnosis of some subtypes of lung cancer according to the WHO Classification.[6] Large cell carcinomas are uncommon undifferentiated non-small cell lung carcinomas that lack morphological, histochemical and immunohistochemical evidence of squamous or glandular differentiation. TTF-1 (for adenocarcinoma), and p40 (for squamous cell carcinoma) are considered the most reliable markers.[46] Immunohistochemical markers are also required, if available, for the diagnosis of solid pattern adenocarcinoma, non-keratinising squamous cell carcinoma and large cell neuroendocrine carcinoma.[6]

Mucinous adenocarcinomas of the lung can exhibit staining for markers that are more commonly associated with carcinomas of the gastrointestinal tract, such as CK20 and CDX-2, and/or fail to stain with markers typically associated with pulmonary carcinoma, such as CK7 and TTF-1.[47] In such cases, exclusion of metastasis from an extrapulmonary primary is best achieved by careful correlation with the radiological distribution of disease and comparison with the primary tumour whenever possible.

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Note 17 – Molecular data (Non-core)

While characterisation of molecular markers is essential in advanced stage disease, they can be performed in resection specimens so that the information is available for treatment decision making if the patient relapses with advanced stage disease. Until recently, clinical treatment was not impacted by the molecular status of early stage tumours. The ADAURA clinical trial demonstrated improved progression free survival in stage IB-IIIA (AJCC 7th edition[48]) resected lung adenocarcinoma patients harbouring *EGFR* exon 19 deletions or L858R mutation treated with adjuvant osimertinib compared to placebo.[49] *EGFR* status in early stage disease may also be important for decisions on adjuvant/neoadjuvant immune checkpoint inhibitors. Clinical trials of other targeted tyrosine kinase inhibitors and other immuno-oncological agents in the adjuvant therapy setting are in progress and it is possible that molecular data may become essential in resected specimens. As specific requirements in early stage disease varies in different countries depending on availability of specific therapies, pathologists should refer to local guidelines for molecular testing requirements.

The number of specific molecular markers required for clinical decision making in the advanced stage setting has expanded and changed over time and varies in different countries depending on availability of specific therapies.

Currently, for de novo presentation of advanced stage non squamous NSCLC, molecular data on the status of *EGFR*, *BRAF*, *MET* exon14, *KRAS*, *ERBB2* (*HER2)*, *RET*, *ALK, ROS1*, and *NTRK1-3* are typically required as a minimum on the basis of currently licensed drugs.[50-52]

Epidermal growth factor receptor (*EGFR*) result

A proportion of lung adenocarcinomas harbours mutations in the epidermal growth factor receptor (*EGFR*) gene that makes them susceptible to the EGFR tyrosine kinase inhibitors (EGFR-TKIs).[53] EGFR-TKIs have been shown to improve progression free, and overall survival in patients with *EGFR*-mutated lung adenocarcinoma

and these agents are established as first line therapy in advanced stage disease in many countries.[54,55] For this reason, the IASLC, College of American Pathologists (CAP) and the Association for Molecular Pathology (AMP) has recommended that patients with advanced stage lung adenocarcinoma have their tumours tested for the presence of EGFR mutations. The *EGFR* testing methodology should follow local/regional or national recommendations; however, the use of multiplex sequencing panels is the preferred method of analysis.[14,50] The guidelines proposed by the IASLC/CAP/AMP also recommend *EGFR* mutational testing to include all advanced stage lung adenocarcinomas.[50,56]

Other molecular data

ALK rearrangements occur in a small subset of lung cancer patients, typically never or light smokers with pulmonary adenocarcinoma, and are associated with response to ALK inhibitors.[57,58-60] *ALK* rearrangements are nearly always mutually exclusive of EGFR and KRAS mutations.[61] Although ALK D5F3 IHC can be used alone to determine patient eligibility for treatment, a common practice is to screen cases with IHC. According to the updated IASLC/CAP/AMP guidelines,[50] IHC is now considered equivalent alternative to FISH ALK testing. Similar to *ALK* rearrangements, c-ros oncogene 1 (*ROS1*) rearrangements have been identified in a small subset of patients and also show response to ROS1 inhibitors.[62] A positive result by ROS1 IHC needs to be confirmed with molecular testing, as false positive IHC results are common.

Expression of PD-L1 protein by IHC is also required in early, locally advanced, and advanced stage NSCLC of squamous or non-squamous histopathology.

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Note 18 – Histologically confirmed distant metastases (Core)

Documentation of known metastatic disease is an important part of the pathology report. If there is evidence in the primary resection specimen of positive metastatic disease such as:

- Separate tumour nodules in a contralateral lobe
- Tumour with pleural or pericardial nodules
- Malignant pleural or pericardial effusion.

Such information should be recorded as ‘at least M1a’ with as much detail as is available, including the site and reference to any relevant prior surgical pathology or cytopathology specimens.

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Note 19 – Pathological staging (Core)

The pathological primary tumour (T) and regional lymph node (N) categories are considered core elements in ICCR datasets. Staging data should be assessed according to the 8th edition of the UICC[2] and AJCC[3] Staging Manuals.

The reference document TNM Supplement: A commentary on uniform use, 5th Edition (C Wittekind et al. editors) may be of assistance when staging.[63]

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