| **Version 3.0 Lung Cancer 3rd revision - published August 2017.** | | | | |
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| **Core/ Non-core** | **Element name** | **Values** | **Commentary** | **Implementation notes** |
| Core | Operative procedure | Single selection value list: • Wedge resection • Segmentectomy • Bilobectomy • Lobectomy • Pneumonectomy • Other (specify) |  |  |
| Core | Specimen laterality | Single selection value list: • Left • Right • Not provided |  |  |
| Core | Attached anatomical structures | Single selection value list: • None submitted • Submitted (describe) |  |  |
| Core | Accompanying specimens | Multi select value list (choose all that apply) • None submitted • Lymph nodes • Other (specify) |  |  |
| Core | Tumour site | Multi select value list (choose all that apply) • Upper lobe  • Middle lobe • Lower lobe • Bronchus (specify site) |  |  |
| Core | Separate tumour nodules | Single selection value list: • Cannot be assessed • Absent • Present • Synchronous primaries | Not infrequently, 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.1,2 Separate tumour nodules of different histologic types are considered synchronous primaries and 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)). For multiple tumour nodules with similar histologies, the criteria of Martini and Melamed have long been used in this distinction.3 According to these criteria, tumours of similar histology are categorized as synchronous primaries if they are in different segments, lobes, or lungs, originate from carcinoma in situ, and there is neither carcinoma in lymphatics common to both nor extrapulmonary metastases at the time of diagnosis.3 More recently, comprehensive histologic assessment has been proposed as a reliable method of separation.4 Although a detailed discussion of this technique is beyond the scope of this document, comprehensive histologic assessment examines not only whether multiple tumours share the same major histologic pattern, but also similarities in the percentages of other histologic patterns and cytologic and stromal features.   Patients with multiple tumour nodules deemed not to represent synchronous primaries 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 deemed not to represent synchronous primaries 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)[1](#_ENREF_1) and American Joint Committee on Cancer (AJCC)[2](#_ENREF_2) to recommend staging such patients similarly.   References  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition, Wiley-Blackwell.  2 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York.  3 Martini M and Melamed MR (1975). Multiple primary lung cancers. J Thorac Cardiovasc Surg 70(4):606-612.  4 Girard N, Deshpande C and Lau C et al (2009). Comprehensive histologic assessment helps to differentiate multiple lung primary nonsmall cell carcinomas from metastases. Am J Surg Pathol 33:1752-1764. | CORE elements should be reported for each synchronous primary.  If present, record the number of tumours and site. |
| Core | Number of tumours | Numeric: \_\_\_ |  |  |
| Core | Site | Multi select value list (choose all that apply) • Same lobe • Different ipsilateral lobe • Contralateral lung |  |  |
| Non-core | Macroscopic appearance of pleura overlying tumour | Text | 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. It is important to note, however, that macroscopic visceral pleural puckering is not itself diagnostic of visceral pleural invasion.1 The presence of visceral pleural invasion must be confirmed histologically.  References  1 Travis WD, Brambilla E, Rami-Porta R, Vallières E, Tsuboi M, Rusch V and Goldstraw P (2008). Visceral pleural invasion: pathologic criteria and use of elastic stains: proposal for the 7th edition of the TNM classification for lung cancer. J Thorac Oncol 3(12):1384–1390. |  |
| Core | Atelectasis/obstructive pneumonitis extending to the hilar region | Single selection value list: • Not assessable • Absent • Present | The presence and extent of atelectasis/obstructive pneumonia factor into assignment of the 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.1 In certain instances, the lack of availability of radiologic information renders this parameter not assessable. In the 8th edition of the UICC2 and AJCC3, the staging impact of atelectasis/obstructive pneumonitis has been modified from the 7th edition, such that 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 categorized as pT2.   References  1 Marchevsky AM (2006). Problems in pathologic staging of lung cancer. Arch Pathol Lab Med. 130(3):292-302.  2 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition, Wiley-Blackwell.  3 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York. |  |
| Core | Maximum tumour dimension | Numeric: \_\_\_mm | Tumour size has long been recognized as an important prognostic indicator in lung cancer.1 Based on survival data, the 8th edition of the TNM system has further subdivided the T category by tumour size.2,3 The maximum diameter of a tumour, measured to the nearest millimetre, should ideally be assessed on the unfixed specimen to avoid the possibility of size underestimation resulting from formalin fixation-induced shrinkage.4 In specimens harbouring multiple synchronous primaries, assignment of the T category is based on the 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.  References  1 Mountain CF, Carr DT and Anderson WA (1974). A system for the clinical staging of lung cancer. Am J Roentgenol Radium Ther Nucl Med. 120:130-138.  2 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition, Wiley-Blackwell.  3 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York.  4 Hsu PK, Huang HC and Hsieh CC et al (2007). Effect of formalin fixation on tumor size determination in stage I non-small cell lung cancer. Ann Thorac Surg 84:1825-1829. |  |
| Core | Tumour involves main bronchus | Single selection value list: • Not applicable • Not assessable • Not identified • Present |  |  |
| Core | Tumour involves carina | Single selection value list: • Not applicable • Not assessable • Not identified • Present | Based on available data, the staging impact of main bronchus involvement has been modified in the 8th edition of TNM staging, such that distance to the carina no longer factors into the pT category designation in tumours that involve the main bronchus without involving the carina. |  |
| Core | Histological tumour type | Multi select value list (choose all that apply) • Squamous cell carcinoma  • Keratinizing  • Non-keratinizing  • Basaloid • Carcinoid  • Typical  • Atypical • Large cell neuroendocrine carcinoma • Large cell carcinoma • Small cell carcinoma • Adenocarcinoma • Other (specify) | All lung carcinomas should be typed according to the 2015 World Health Organisation (WHO) Classification (see list below).1 Accurate typing of lung carcinoma is becoming increasingly important, as histology impacts on decisions to proceed with molecular testing (see below) and the most appropriate chemotherapy regimen for patients in whom adjuvant therapy is indicated. 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.2 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 poorly differentiated cases, immunohistochemistry can greatly aid in classification.   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) requires that lesions be entirely submitted for histopathologic examination.2   It should be noted that the recommendations put forth in this document apply 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 has since also been scientifically validated for small cell carcinoma and carcinoid tumours.3   World Health Organisation classification of tumours of the lung1   References  1 WHO (World Health Organization) (2015). WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Fourth edition Travis WD, Brambilla E, Burke AP, Marx A and Nicholson AG. IARC Press, Lyon, France.  2 Travis WD, Brambilla E and Noguchi M et al (2011). International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 6:244-285.  3 Shepherd FA, Crowley J, Van Houtte P, Postmus PE, Carney D, Chansky K, Shaikh Z and Goldstraw P (2007). The International Association for the Study of Lung Cancer lung cancer staging project: proposals regarding the clinical staging of small cell lung cancer in the forthcoming (seventh) edition of the tumor, node, metastasis classification for lung cancer. J Thorac Oncol 2(12):1067–1077. | Value list from the World Health Organisation Classification of Tumours. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. (2015) Note that permission to publish the WHO classification of tumours may be needed in your implementation. It is advisable to check with the International Agency on Cancer research (IARC).  If adenocarcinoma, record the classification of adenocarcinoma |
| Core | Classification of adenocarcinoma | Select all that apply: • Adenocarcinoma in situ (AIS)   o Non-mucinous   o Mucinous   • Minimally invasive adenocarcinoma (MIA)   o Non-mucinous   o Mucinous   • Invasive adenocarcinoma  Predominant pattern   o Lepidic   o Acinar   o Papillary   o Micropapillary   o Solid   o Invasive mucinous   o Colloid   o Fetal   o Enteric |  | For the predominant pattern, record the %. |
| Non-core |  | • Invasive adenocarcinoma   Other patterns (if present) (specify each type and its percentage) |  |  |
| Core | Percentage |  |  |  |
| Core | Distance of tumour to closest resection margin | Numeric: \_\_\_mm | Although level III-2 and above evidence 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 visualized 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. |  |
| Non-core | Histological grade | Single selection value list: • Well differentiated • Moderately differentiated • Poorly differentiated • Undifferentiated • Not applicable | Although a tiered grading scheme for lung cancer is specified by the AJCC, its reproducibility and prognostic significance has not been rigorously tested.1 According to the WHO, sarcomatoid carcinomas (pleomorphic carcinoma, spindle cell carcinoma, giant cell carcinoma, and carcinosarcoma) and pulmonary blastoma are classified as high grade (poorly differentiated) and large cell carcinoma is classified as undifferentiated. However, a definitive grading system for resected lung adenocarcinomas has yet to be established and there are insufficient data to determine how to grade squamous and adenosquamous carcinoma and as such, these tumours can be assigned the ‘not applicable’ category.2 Alternatively, for lung adenocarcinoma one grading system that has been proposed by the International Association for the Study of Lung Cancer (IASLC), American Thoracic Society (ATS) and European Respiratory Society (ERS) but has not yet been formally adopted is based on the predominant histologic subtype and has been shown to correlate with prognosis.3-5 In this scheme, lepidic-predominant tumours (grade 1) correspond to well-differentiated tumours, acinar or papillary-predominant tumours (grade 2) behave as moderately differentiated tumours, and solid or micropapillary-predominant tumours (grade 3) would be considered poorly differentiated tumours.2 Cribriform predominant tumours are currently classified alongside acinar predominant tumours as G2, but may show worse prognosis. Invasive mucinous adenocarcinoma and colloid adenocarcinoma are classified as G3. In tumours that exhibit more than one grade of differentiation, the grade of the least differentiated component should be reported as the histological grade. The WHO Classification of Lung, Pleura, Thymus and Heart should be consulted for the applicability and/or assignment of histologic grade for tumours not discussed here.  References  1 Chung CK, Zaino R, Stryker JA, O'Neill M J and DeMuth WE Jr (1982). Carcinoma of the lung: evaluation of histological grade and factors influencing prognosis. Ann Thorac Surg 33:599-604.  2 WHO (World Health Organization) (2015). WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Fourth edition Travis WD, Brambilla E, Burke AP, Marx A and Nicholson AG. IARC Press, Lyon, France.  3 Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger K, Yatabe Y, Powell CA, Beer D, Riely G, Garg K, Austin JH, Rusch VW, Hirsch FR, Jett J, Yang PC and Gould M (2011). International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society: international multidisciplinary classification of lung adenocarcinoma: executive summary. Proc Am Thorac Soc 8(5):381-385.  4 Tsuta K, Kawago M, Inoue E, Yoshida A, Takahashi F, Sakurai H, Watanabe S, Takeuchi M, Furuta K, Asamura H and Tsuda H (2013). The utility of the proposed IASLC/ATS/ERS lung adenocarcinoma subtypes for disease prognosis and correlation of driver gene alterations. Lung Cancer 81(3):371-376.  5 Yoshizawa A, Motoi N and Riely GJ et al (2011). Impact of proposed IASLC/ATS/ERS classification of lung adenocarcinoma: prognostic subgroups and implications for further revision of staging based on analysis of 514 stage I cases. Mod Pathol 24:653-664. |  |
| Core | Response to neoadjuvant therapy | Single selection value list: • Not applicable • Less than 10% residual viable tumour  • Greater than 10% residual viable tumour • Treatment history not known | Quantification of the extent of tumour regression in patients who have received neoadjuvant chemotherapy and/or radiation therapy is prognostically useful.1,2 An estimation of whether greater or less than 10% residual viable tumour is present in the resection specimen should be reported and the “y” prefix included as part of the TNM pathologic stage.  References  1 Junker K, Langer K, Klinke F, Bosse U and Thomas M (2001). Grading of tumor regression in non-small cell lung cancer: morphology and prognosis. Chest 120(5):1584-1591.  2 Pataer A, Kalhor N and Correa AM et al (2012). Histopathologic Response Criteria Predict Survival of Patients with Resected Lung Cancer After Neoadjuvant Chemotherapy. J Thorac Oncol. |  |
| Core | Direct invasion of adjacent structures | • Not identified • Not applicable  OR Multi select value list (select all that apply): • Trachea  • Chest wall • Diaphragm • Oesophagus • Heart • Great vessels  • Vertebral body • Phrenic nerve  • Mediastinum  • Mediastinal fat  • Mediastinal pleura  • Parietal pericardium • Recurrent laryngeal nerve | Extension of tumour into extrapulmonary structures is an adverse prognostic factor, the degree of which depends on the structures involved.1,2 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.   References  1 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition, Wiley-Blackwell.  2 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York. |  |
| Core | Lymphovascular invasion | Single selection value list: • Not identified • Indeterminate • Present | Lymphovascular invasion has been demonstrated to be an independent prognostic factor in lung carcinoma and is an exclusionary criterion for the new entities of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA).1-5 A number of studies has evaluated the prognostic impact of large vessel (arterial and/or venous) invasion independent of lymphatic invasion with somewhat conflicting results.6-8 For this reason, it is permissible to report the presence of vascular and/or lymphatic invasion under the single heading of lymphovascular invasion.   References  1 Bréchot JM, Chevret S, Charpentier MC, Appere de Vecchi C, Capron F, Prudent J, Rochemaure J and Chastang C (1996). Blood vessel and lymphatic vessel invasion in resected nonsmall cell lung carcinoma. Correlation with TNM stage and disease free and overall survival. Cancer 78(10):2111–2118.  2 Gabor S, Renner H, Popper H, Anegg U, Sankin O, Matzi V, Lindenmann J and Smolle Jüttner FM (2004). Invasion of blood vessels as significant prognostic factor in radically resected T1-3N0M0 non-small-cell lung cancer. European Journal of Cardio-Thoracic Surgery 25(3):439–442.  3 Rigau V, Molina TJ, Chaffaud C, Huchon G, Audouin J, Chevret S and Brechot JM (2002). Blood vessel invasion in resected non small cell lung carcinomas is predictive of metastatic occurrence. Lung Cancer 38(2):169–176.  4 Miyoshi K, Moriyama S, Kunitomo T and Nawa S (2009). Prognostic impact of intratumoral vessel invasion in completely resected pathologic stage I non-small cell lung cancer. Journal of Thoracic and Cardiovascular Surgery 137(2):429–434.  5 WHO (World Health Organization) (2015). WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart. Fourth edition Travis WD, Brambilla E, Burke AP, Marx A and Nicholson AG. IARC Press, Lyon, France.  6 Pechet TT, Carr SR, Collins JE, Cohn HE and Farber JL (2004). Arterial invasion predicts early mortality in stage I non-small cell lung cancer. Ann Thorac Surg 78:1748-1753.  7 Yilmaz A, Duyar SS and Cakir E et al (2011). Clinical impact of visceral pleural, lymphovascular and perineural invasion in completely resected non-small cell lung cancer. Eur J Cardiothorac Surg. 40:664-670.  8 Shimada Y (2010). Extratumoral vascular invasion is a significant prognostic indicator and a predicting factor of distant metastasis in non-small cell lung cancer. J Thorac Oncol 5:970-975. |  |
| Core | Visceral pleural invasion | Single selection value list: • Cannot be assessed • Indeterminate • Not identified • Present | The presence of tumour at the surface of the visceral pleura has been recognized as an independent adverse prognostic factor for quite some time.1 More recently, penetration through the visceral pleural elastic layer was shown to have the same prognostic impact.2,3 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.4 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.   Often, there is not one, but 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. It is the recommendation of the International Staging Committee that the thickest elastic layer be used to assess VPI.4 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 is 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).5 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 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 categorized as T2.4     References  1 Mountain CF, Carr DT and Anderson WA (1974). A system for the clinical staging of lung cancer. Am J Roentgenol Radium Ther Nucl Med. 120:130-138.  2 Shimizu K, Yoshida J and Nagai K et al (2004). Visceral pleural invasion classification in non-small cell lung cancer: a proposal on the basis of outcome assessment. J Thorac Cardiovasc Surg. 127(6):1574-1578.  3 Osaki T, Nagashima A, Yoshimatsu T, Yamada S and Yasumoto K (2004). Visceral pleural involvement in nonsmall cell lung cancer: prognostic significance. Ann Thorac Surg 77:1769-1773.  4 Travis WD, Brambilla E, Rami-Porta R, Vallières E, Tsuboi M, Rusch V and Goldstraw P (2008). Visceral pleural invasion: pathologic criteria and use of elastic stains: proposal for the 7th edition of the TNM classification for lung cancer. J Thorac Oncol 3(12):1384–1390.  5 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York. | If present, record extent of pleural involvement |
| Non-core | Extent of pleural involvement | Single selection value list: • PL1 • PL2 • PL3 | Although tumour penetration beyond the visceral pleural elastic layer has been shown to have the same prognostic significance as tumour extending to the visceral pleural surface (see above), the pathologist may wish to provide greater detail in the report by documenting the extent of pleural invasion. A scheme for classifying pleural involvement by tumour put forth by Hammar, which has been recognised by the Japan Lung Society and recently undergone slight modification by the International Staging Committee, is as follows:   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.1,2   PL0 is categorized 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 categorized as T1 or T2 are changed to T3 in the presence of type PL3 pleural involvement.1,3,4   References  1 Travis WD, Brambilla E, Rami-Porta R, Vallières E, Tsuboi M, Rusch V and Goldstraw P (2008). Visceral pleural invasion: pathologic criteria and use of elastic stains: proposal for the 7th edition of the TNM classification for lung cancer. J Thorac Oncol 3(12):1384–1390.  2 Dail DH and Hammar SP (eds) (1994). Pulmonary Pathology. 2nd ed, Springer-Verlag, New York.  3 Brierley JD, Gospodarowicz MK and Wittekind C (eds) (2016). UICC TNM Classification of Malignant Tumours, 8th Edition, Wiley-Blackwell.  4 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York. |  |
| Non-core | Perineural invasion | Single selection value list: • Not identified • Indeterminate • Present |  |  |
| Non-core | Other neoplastic processes (eg tumourlets,NEH, AAH, dysplasia) | Text |  |  |
| Non-core | Non-neoplastic lung disease | Text |  |  |
| Core | SURGICAL MARGIN STATUS |  | Completeness of resection is not only an important prognostic factor, but also influences post-operative management, including decisions about adjuvant therapy.1 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. 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.2-5 Recently, however, the significance of peribronchial soft tissue involvement without mucosal involvement has been called into question.6 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 carcinoma in situ (CIS) at the bronchial margin remains unresolved due to its rare occurrence.7 Results of several studies suggest the presence of CIS at the margin is not an independent prognostic factor.7,8 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.  References  1 Rami-Porta R, Mateu-Navarro M and Freixinet J et al (2005). Type of resection and prognosis in lung cancer. Experience of a multicentre study. Eur J Cardiothorac Surg 28:622-628.  2 Soorae AS and Stevenson HM (1979). Survival with residual tumor on the bronchial margin after resection for bronchogenic carcinoma. J Thorac Cardiovasc Surg 78:175-180.  3 Snijder RJ, Brutel de la Riviere A, Elbers HJ and van den Bosch JM (1998). Survival in resected stage I lung cancer with residual tumor at the bronchial resection margin. Ann Thorac Surg 65:212-216.  4 Kawaguchi T, Watanabe S, Kawachi R, Suzuki K and Asamura H (2008). The impact of residual tumor morphology on prognosis, recurrence, and fistula formation after lung cancer resection. J Thorac Oncol 3:599-603.  5 Kaiser LR, Fleshner P, Keller S and Martini N (1989). Significance of extramucosal residual tumor at the bronchial resection margin. Ann Thorac Surg 47:265-269.  6 Sakai Y, Ohbayashi C and Kanomata N et al (2011). Significance of microscopic invasion into hilar peribronchovascular soft tissue in resection specimens of primary non-small cell lung cancer. Lung Cancer 73:89-95.  7 Vallieres E, Van Houtte P, Travis WD, Rami-Porta R and Goldstraw P (2011). Carcinoma in situ at the bronchial resection margin: a review. J Thorac Oncol. 6:1617-1623.  8 Wind J, Smit EJ, Senan S and Eerenberg JP ( 2007). Residual disease at the bronchial stump after curative resection for lung cancer. Eur J Cardiothorac Surg 32:29-34. | Header |
| Core | Bronchial margin | Single selection value list: • Not applicable • Not involved • Involved by invasive carcinoma • Involved by CIS only • Only peribronchial soft tissue involved |  |  |
| Core | Vascular margin | Single selection value list: • Not applicable • Not involved • Involved • Only perivascular soft tissue involved |  |  |
| Core | Other margin 1 eg parenchymal, chest wall | Text (specify margin) AND Single selection value list: • Not applicable • Not involved • Involved |  | Repeat for each other margin |
| Core | Lymph node status | Single selection value list: • Not involved • Involved • Involved by micrometastasis only | Lymph node metastases are an adverse prognostic factor, the extent of which is dependent on the location of the involved lymph nodes.1 The site(s) of involvement (lymph node stations) should be recorded according to the IASLC lymph node map.2 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 it be quantified. Otherwise, it is permissible to report the sites of nodal metastases without specifying the number involved. Cases with only micrometastasis (greater than 0.2 mm but less than or equal to 0.2 cm) to lymph nodes can be classified 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.   References  1 Rusch VW, Crowley J, Giroux DJ, Goldstraw P, Im J-G, Tsuboi M, Tsuchiya R and Vansteenkiste J (2007). The IASLC Lung Cancer Staging Project: proposals for revision of the N descriptors in the forthcoming (seventh) edition of the TNM classification of lung cancer. J Thorac Oncol 2(7):603–612.  2 Amin MB, Edge SB and Greene FL et al (eds) (2017). AJCC Cancer Staging Manual. 8th ed., Springer, New York. | If involved, record the number of involved nodes and total number of nodes per station. |
| Core | Station(s) examined (specify) | Text |  |  |
| Core | Involved station (specify) | Text |  | Repeat for each involved station |
| Core | Number of involved lymph nodes | Numeric: \_\_\_ OR Number cannot be determined |  | For this involved site |
| Core | Total number of lymph nodes from this site | Numeric: \_\_\_ |  | For this involved site |
| Non-core | ANCILLARY STUDIES |  |  | Header |
| Non-core | Immunohistochemical markers | List (as applicable): • Positive antibodies • Negative antibodies • Equivocal antibodies | A concerted effort should be made to classify poorly differentiated lung cancers in resection specimens. There have been a number of studies examining the best means for doing so using an immunohistochemical approach, which have shown TTF-1, napsin, CK5/6 and p63 to be among the most reliable markers.1,2 p40, an antibody against an isoform of p63, has recently been reported to be a highly specific marker for squamous cell carcinoma.3   Mucinous adenocarcinomas of the lung can exhibit aberrant 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-1.4 In such cases, exclusion of metastasis from an extrapulmonary primary is best achieved by careful correlation with the radiological distribution of disease.  References  1 Terry J, Leung S, Laskin J, Leslie KO, Gown AM and Ionescu DN (2010). Optimal immunohistochemical markers for distinguishing lung adenocarcinomas from squamous cell carcinomas in small tumor samples. Am J Surg Pathol. 34:1805-1811.  2 Mukhopadhyay S and Katzenstein AL (2011). Subclassification of non-small cell lung carcinomas lacking morphologic differentiation on biopsy specimens: Utility of an immunohistochemical panel containing TTF-1, napsin A, p63, and CK5/6. Am J Surg Pathol 35:15-25.  3 Bishop JA, Teruya-Feldstein J, Westra WH, Pelosi G, Travis WD and Rekhtman N (2012). p40 (DeltaNp63) is superior to p63 for the diagnosis of pulmonary squamous cell carcinoma. Mod Pathol 25:405-415.  4 Rossi G, Murer B and Cavazza A et al (2004). Primary mucinous (so-called colloid) carcinomas of the lung: a clinicopathologic and immunohistochemical study with special reference to CDX-2 homeobox gene and MUC2 expression. Am J Surg Pathol 28:442-452. |  |
| Non-core | Conclusions | Text |  |  |
| Non-core | Molecular data |  | 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) erlotinib and gefitinib.1,2 EGFR-TKIs have been shown to improve progression-free survival in patients with EGFR-mutated lung adenocarcinoma and these agents are being considered as first line therapy in advanced stage disease in many countries.3 For this reason, the IASLC/ATS/ERS has recommended that patients with advanced stage lung adenocarcinoma have their tumours tested for the presence of EGFR mutations, with DNA sequencing as the preferred method of analysis.4 The guidelines proposed by the College of American Pathologists (CAP), the International Association for the Study of Lung Cancer (IASLC), and the Association for Molecular Pathology (AMP) expand the recommendation for EGFR mutational testing to include all lung adenocarcinomas.5,6 The EGFR methodology should follow local/regional or national recommendations.   Other molecular data  KRAS mutations, and EML4-ALK rearrangements are but a few of the continuously expanding array of molecular alterations other than EGFR that have prognostic and/or therapeutic implications in lung cancer.   Mutations in KRAS may be associated with a lack of response to EGFR-TKIs.7 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 such as crizotinib.8,9 ALK rearrangements are nearly always mutually exclusive of EGFR and KRAS mutations.10 Similar to ALK rearrangements c-ros oncogene 1 (ROS1) rearrangements have been identified in a small subset of patients and also show response to crizotinib.11 The National Comprehensive Cancer Network (NCCN) has recommended that patients with advanced stage non-squamous non-small cell carcinoma be tested not only for EGFR mutations, but also for ALK rearrangements.12 In the U.S., the Food and Drug Administration (FDA)-approved methods for EML4-ALK rearrangement testing include fluorescence in situ hybridization (FISH) using a break-apart probe and most recently, Ventana ALK D5F3 immunohistochemistry to aid in the identification of patients eligible for crizotinib.13,14 Although the package insert for crizotinib indicates that as an FDA-approved method, ALK D5F3 can be used alone to determine patient eligibility for treatment, a common practice is to screen cases with immunohistochemistry and proceed to FISH only in cases that are equivocal or positive by immunohistochemistry for confirmation of the ALK status.     References  1 Paez JG, Janne PA and Lee JC et al (2004). EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. Science 304:1497-1500.  2 Pao W, Miller V and Zakowski M et al (2004). EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. Proceedings of the National Academy of Sciences of the United States of America 101:13306-13311.  3 Azzoli CG, Baker Jr S, Temin S, Pao W, Aliff T, Brahmer J, Johnson DH and Laskin JL et al (2009). American Society of Clinical Oncology Clinical Practice Guideline Update on Chemotherapy for Stage IV Non–Small-Cell Lung Cancer. J Clin Oncol 27:6251-6266.  4 Travis WD, Brambilla E and Noguchi M et al (2011). International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol 6:244-285.  5 Cagle PT and Chirieac LR (2012). Advances in treatment of lung cancer with targeted therapy. Arch Pathol Lab Med 136:504-509.  6 Lindeman NI, Cagle PT, Beasley MB, Chitale DA, Dacic S, Giaccone G, Jenkins RB, Kwiatkowski DJ, Saldivar JS, Squire J, Thunnissen E and Ladanyi M (2013). Molecular Testing Guideline for Selection of Lung Cancer Patients for EGFR and ALK Tyrosine Kinase Inhibitors: Guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology. J Thorac Oncol. 8(7):823-859.  7 Pao W, Wang TY and Riely GJ et al (2005). KRAS mutations and primary resistance of lung adenocarcinomas to gefitinib or erlotinib. PLoS Med. 2:e17.  8 Shaw AT, Yeap BY and Mino-Kenudson M et al (2009). Clinical features and outcome of patients with non-small-cell lung cancer who harbor EML4-ALK. J Clin Oncol 27:4247-4253.  9 Kwak EL, Bang YJ and Camidge DR et al (2010). Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med 363:1693-1703.  10 Soda M, Choi YL and Enomoto M et al (2007). Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. Nature 448:561-566.  11 Shaw AT, Ou SH, Bang YJ, Camidge DR, Solomon BJ, Salgia R, Riely GJ, Varella-Garcia M, Shapiro GI, Costa DB, Doebele RC, Le LP, Zheng Z, Tan W, Stephenson P, Shreeve SM, Tye LM, Christensen JG, Wilner KD, Clark JW and Iafrate AJ (2014). Crizotinib in ROS1-rearranged non-small-cell lung cancer. N Engl J Med 371(21):1963-1971.  12 NCCN Clinical Practice Guidelines in Oncology (2012). Non-Small-Cell Lung Cancer. Version 2. http://www.nccn.org/professionals/physician\_gls/pdf/nscl.pdf.  13 Shaw AT, Solomon B and Kenudson MM (2011). Crizotinib and testing for ALK. J Natl Compr Canc Netw. 9:1335-1341.  14 Ventana Medical Systems Inc (2015). Media Release: Ventana receives FDA approval for the first fully automated IHC companion diagnostic to identify lung cancer patients eligible for XALKORI® (crizotinib). http://www.ventana.com/site/page?view=press-release-jun15-2015. Accessed 20th May 2017 | Heading |
| Non-core | EGFR result | Single selection value list: • Mutation absent • Mutation present • Result indeterminate |  | If present, describe |
| Non-core | Describe | Text |  |  |
| Non-core | EML4-ALK result | Single selection value list: • Rearrangement absent • Rearrangement present • Result indeterminate |  | If present, describe |
| Non-core | Describe | Text |  |  |
| Non-core | Other (specify) | Text |  | For each other test, record test and results |
| Non-core | Test | Text |  |  |
| Non-core | Result | Text |  |  |
| Core | Pathological staging (TNM 8th edition) |  | The reference document: TNM Supplement: A commentary on uniform use, 4th Edition ( C Wittekind editor) may be of assistance when staging.1 References 1 Wittekind C (ed) (2012). TNM Supplement : A Commentary on Uniform Use, The Union for International Cancer Control (UICC), Wiley-Blackwell. | Header.   Note that permission to publish the TNM cancer staging tables may be needed in your implementation. It is advisable to check. |
| Core | Suffixes | Choose if applicable: • 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 |  |  |
| Core | T -Primary tumour | Per 8th edition |  |  |
| Core | N - Regional lymph nodes | Per 8th edition |  |  |
| Core | M - Distant metastasis | Per TNM 8th edition or Not applicable |  |  |