LIDC Pathology Group

Prepared by the LIDC Pathology Committee - July 2002.

Process

The pathology/cytology classification status will be maintained as part of the LIDC web site as an accessible database, with accessibility to study pathologists. The process will be as follows:
The case undertaking radiology studies will be ascribed a study number.
The site submitting the radiology for the case will be responsible for the pathology record of the case, or in the instance of no change with prolonged followup, for maintaining a record indicating a likely benign process.
The pathology of record will be maintained at one of the five LIDC study sites, in a file marked and maintained as a LIDC study subject.
The LIDC study pathologist will review accrued pathology slides on a monthly basis, and enter the findings in the web based database.
At 3 monthly intervals, commencing January 1 of each year, the accrued pathology slides will be distributed to one of the other 4 participating LIDC centers, for pathology review. The second pathology review will be entered onto the web site, without prior knowledge of the first review conclusions. This second review will be concluded within 6 weeks.
The pathology group convener/co-convener will then review the database for concordance, just prior to the end of the three month period.. Non concordant cases will be distributed to one of the LIDC consulting referees (Dr Travis or Noguchi). A 6 week turn around is expected.
The pathology group will meet annually together with the LIDC consulting referees to review progress, and resolve or define continuing conflicts.
Sites that are not LIDC sites, but who are collecting CT data that will populate the LIDC database, will be allocated to work through one of the LIDC sites. In this instance, by mutual arrangement the pathology of record will still be reviewed by LIDC study pathologists, but maintained as part of the records of the contributing site.
All entries into the database will be anonymized. The pathogy slides that are reviewed will only be identified by a local pathology laboratory number, and the LIDC study number.
In case of clinically important information arising from the pathology review, during the study the pathology group convener/co-convener will notify the LIDC institution of record PI.

Rules for Classification and handling of lung tumors

1. Use 1999 WHO classification (see below).
2. Each site to use their standard protocol for handling of specimens and which should include:
    i. Blocking and processing of all tumor tissue.
    ii. Banking fresh frozen tumor and normal lung.
    iii. Keeping track of all lesions and location of blocks, including distance from tumor.
    iv. Measuring extent of scar, invasion, lepidic growth.
    v. Determining vascular and pleural invasion.
3. Lesions 3 cm or less, with a central scar are classified as adenocarcinoma. To make a diagnosis of bronchiolo-alveolar carcinoma, there should be no tissue invasion or scar.
4. The size of the scar (<0.5 cm), percent of lepidic growth (>75%), vascular invasion and papillary growth component (>25%) appear to be independent prognostic factors.

References:

1) Noguchi M, Morikawa A, Kowasaki M, Matsuno Y, Yamada T, Hirohashi S, Kondo H, Shimosato Y. Small adenocarcinoma of the lung: histologic characteristics and Prognosis. *Cancer* 1995;75:2844-52.

2) Suzuki, K, Yokose T, Yoshida J, Nishimura M, Takahashi K, Nagai K, Nishiwaki Y. Prognostic significance of the size of central fibrosis in peripheral adenocarcinoma of the lung. *Ann Thorac Surg* 2000;69:893-7.

3) Yokose T, Suzuki K, Nagai K, Nishiwaki Y, Sasaki S, Ochiai A. Favorable and unfavorable morphological prognostic factors in peripheral adenocarcinoma of the lung 3 cm or less in diameter. *Lung Cancer* 2000;29179-88.

Cytology Classification

Cytologic material must be reviewed in all those cases in which it forms the basis for final pathologic diagnosis. This would include any of the following from retrospective and prospective cases in the study:

- Fine needle aspiration (FNA)
- Bronchial brushing and washing
- Pleural fluid

All diagnostic material will be reveiwed by two subcommittee pathologists, each from a different institution. No further action is needed if there is complete agreement on the diagnosis. In those cases where there is disagreement, a third pathologist (from a third institution) will review, discuss with initial pathologists and issue the final diagnosis.

Since the WHO classification is not applicable to cytologic material, the case will be placed into one of the following categories:

- Benign
- Malignant, small cell carcinoma or non-small cell carcinoma
- Malignant, other

Benign Tumors

1. Measure size, process completely, sample uninvolved lung and any other lesion.
2. Classify according to WHO classification.

LIDC Pathology Data Accrual Form

LIDC Identifier:

Pathology Group Identifier:

Pathology Data:

A. Histopathologic Type:
   1. Epithelial Tumors

	1.1	*Benign*		
?	l.1.1	Papillomas		8050/0
?	1.1.1.1	Squamous cell papilloma	8052/0	
?	1.1.1.2	Glandular papilloma		8260/0
?	1.1.1.3	Mixed squamous cell and glandular papilloma	8560/0	
?	1.1.2	Adenomas		8140/0
?	1.1.2.1	Alveolar adenoma		8251/0
?	1.1.2.2	Papillary adenoma		8260/0
?	1.1.2.3	Adenomas of salivary gland type		
?	1.1.2.3.1	Mucous gland adenoma	8140/0	
?	1.1.2.4	Pleomorphic adenoma		8940/0
	1.2	*Preinvasive lesions*		
?	1.2.1	Squamous dysplasia		74000
?	1.2.2	Atypical adenomatous hyperplasia	72425	
?	1.2.3.	Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia		
	1.3	*Malignant*		
?	1.3.1	Squamous cell carcinoma	8070/3	
?	1.3.2	Small cell carcinoma		8041/3
?	1.3.2.1	Combined small cell carcinoma	8045/3	
?	1.3.3	Adenocarcinoma _____ scar size _____ percent growth _____ papillary growth component	8140/3	
?	1.3.3.3	Bronchioloalveolar carcinoma	8250/3	
?	1.3.4	Large cell carcinoma		8012/3
?	1.3.5	Adenosquamous carcinoma		8560/3
?	1.3.6	Carcinomas with pleomorphic, sarcomatoid or sarcomatous elements		8030/3
?	1.3.7	Carcinoid tumor	8240/3	
?	1.3.8	Carcinomas of salivary gland type		
?	1.3.9	Unclassified carcinomas	8010/3	

2. Soft Tissue Tumors

?	2.1	Localized fibrous tumor	8815/0	
?	2.2	Epithelioid hemangioendothelioma	9133/1	
?	2.3	Pleuropulmonary blastoma		8973/3
?	2.4	Chondroma		9220/0
?	2.5	Calcifying fibrous pseudotumor of the pleura		
?	2.6	Congenital peribronchial myofibroblastic tumor	8827/1	
?	2.7	Diffuse pulmonary lymphangiomatosis	9176/1	
?	2.8	Desmoplastic round cell tumor	8806/3	
?	2.9	Others		

3. Mesothelial Tumors

	3.1	*Benign*		
?	3.1.1	Adenomatoid tumor		

?	3.2	Malignant mesothelioma		
4.	Miscellaneous Tumors			
?	2.3	Hamartoma		75500
?	2.4	Sclerosing hemangioma	8832/0	
?	2.5	Clear Cell Tumor	8005/0	
?	2.6	Germ Cell Tumors		
?	2.7	Thymoma		8580/1
?	2.8	Malignant Melanoma		8720/3
?	2.9	Others		
5.	Lymphoproliferative Diseases			
?	5.1	Lymphoid interstitial pneumonia (LIP)	43130	
?	5.2	Nodular lymphoid hyperplasia	72290	
?	5.3	Low grade marginal zone B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT)	9699/3	
?	5.4	Lymphomatoid granulomatosis	9680/3	
6.	Secondary Tumors			
7.	Unclassified Tumors			

8. Tumor-like Lesions

?	8.1	Tumorlet		8040/0
?	8.3	Langerhans cell histiocytosis		44050
?	8.4	Inflammatory pseudotumor (inflammatory		
?		myofibroblastic tumor)	7682/0	
?	8.5	Localized organizing pneumonia	45000	
?	8.6	Amyloid tumor	55160	
?	8.7	Hyalinizing granuloma		
?	8.8	Lymphangioleiomyomatosis		9174/1
?	8.12	Others		

B. Histologic Grade

? Well differentiate
? Moderately differentiated
? Poorly differentiated
? Cannot grade

C. Tumor Size (see report): _____

D. T Classification

? **TX:** Primary tumor cannot be assessed, or tumor proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy.
? **T0:** No evidence of primary tumor.
? **Tis:** Carcinoma *in situ*
? **T1:** Tumor 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)
? **T2:** Tumor with any of the following features of size or extent:
- More than 3 cm in greatest dimension
- Involves main bronchus, 2 cm or more distal to the carina
- Invades the visceral pleura
- Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung.

? **T3:** Tumor of any size that directly invades any of the following: chest wall (including superior sulcus tumors), diaphragm, mediastinal pleura, parietal pericardium; or tumor in the main bronchus less than 2 cm distal to the carina, but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung.
? **T4:** Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, esophagus, vertebral body, carina; or separate tumor nodules in the same lobe; or tumor with malignant pleural effusion.**

***Note:** The uncommon superficial tumor of any size with its invasive component limited to the bronchial wall, which may extend proximal to the main bronchus, is also classified T1.

****Note:** Most pleural effusions associated with lung cancer are due to tumor. However, there are a few patients in whom multiple cytopathologic examinations of pleural fluid are negative for tumor. In these cases, fluid is non-bloody and is not an exudate. Such patients may be further evaluated by videothoracoscopy (VATS) and direct pleural biopsies. When these elements and clinical judgment dictate that the effusion is not related to the tumor, the effusion should be excluded as a staging element and the patient should be staged T1, T2 or T3.

E. N Classification:

? **NX:** Regional lymph nodes cannot be assessed.
? **N0:** No regional lymph node metastasis.
? **N1:** Metastasis to ipsilateral peribronchial and/or ipsilateral hilar lymph nodes, and intrapulmonary nodes including involvement by direct extension of the primary tumor.
? **N2:** Metastasis to ipsilateral mediastinal and/or subcarinal lymph nodes(s).
? **N3:** Metastasis to contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph nodes(s).

F. Lymphovascular Space Invasion:
? Identified
? Not identified

G. Margin Status
1. Bronchial
? Positive
? Negative

2. Pleural
? Positive
? Negative
? Not applicable

3. Other _____
? Positive
? Negative

H. Pleural Invasion
? Present
? Absent

I. Other Comments