CHEST Special Feature

# The New Lung Cancer Staging System

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**The International Association for the Study of Lung Cancer (IASLC) has conducted an extensive initiative to inform the revision of the lung cancer staging system. This involved development of an international database along with extensive analysis of a large population of patients and their prognoses. This article reviews the recommendations of the IASLC International Staging Committee for the definitions for the TNM descriptors and the stage grouping in the new non-small cell lung cancer staging system.** ***(CHEST 2009; 136:260–271)***

**Abbreviations:** AJCC = American Joint Committee on Cancer; IASLC = International Association for the Study of Lung Cancer; NSCLC = non-small cell lung cancer; SEER = Surveillance, Epidemiology, and End Results; UICC = Union Internationale Contre le Cancer

Definition of the stage is an essential part of the approach to patients with cancer, and it has led to the development of a universally accepted stage classification systems for most tumors. The Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC) serve as the official bodies that define, periodically review, and refine the stage classification systems. The 6th edition of the staging system was published in 2002,[1] and the 7th edition will be published in 2009. In preparation for this, much work has been done by the International Association for the Study of Lung Cancer (IASLC) to recommend changes that are based on a large international database and are backed by careful validation and statistical analysis. This article reviews the development and final recommendations of the IASLC International Staging Committee for non-small cell lung cancer (NSCLC), which have been accepted by the UICC and AJCC for the new edition.

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The TNM staging system for lung cancer dates back to an initial proposal by Dr. Clifton Mountain that was adopted by the AJCC in 1973 and by the UICC in 1974. The original system was based heavily on intuition with limited corroboration from a database of 2,155 patients from the MD Anderson Cancer Center in Houston, TX. Subsequent revisions of the TNM staging system continued to be based on this database, which grew to include 5,319 cases at the time the lung cancer staging system was last revised in 1997. The limitations of this system are that it was based on what was essentially a single institution series, included a limited number of patients (so that many subgroups were quite small), spanned a long time frame, and was weighted somewhat toward surgically treated patients by the nature of the database. Nevertheless, this early work laid a significant foundation and defined a staging system that has held up very well even in comparison with the new IASLC staging system.

## Fundamentals of the UICC/AJCC Staging System

The NSCLC stage classification is based on the TNM system, which is used for most cancers. The T descriptor defines the extent of the primary tumor,

**Table 1—*Types of Staging Assessments***

| Prefix | Name | Definition |
|---|---|---|
| c | Clinical | Prior to initiation of any treatment, using any and all information available (*eg*, including mediastinoscopy) |
| p | Pathologic | After resection, based on pathologic assessment |
| y | Restaging | After part or all of the treatment has been given |
| r | Recurrence | Stage at time of a recurrence |
| a | Autopsy | Stage as determined by autopsy |

**Table 2—*Residual Tumor After Treatment***

| Symbol | Name | Definition |
|---|---|---|
| R0 | No residual | No identifiable tumor remaining; negative surgical margins |
| R1 | Microscopic residual | Microscopically positive margins but no visible tumor remaining |
| R2 | Gross residual | Gross (visible or palpable) tumor remaining |

the N descriptor the extent of involvement of regional lymph nodes, and the M descriptor the extent of spread to distant sites. The staging system is based solely on the anatomic extent of disease. Other factors, such as clinical symptoms or molecular biological characterization of the tumor, have not been included. Increasing T status reflects tumors that are larger or invasive into more peripheral (*ie*, visceral pleura, chest wall) or more central structures (*ie*, lobar or mainstem bronchus, mediastinum). In lung cancer, nodal staging depends on the location of involved nodes (as opposed to the number of nodes). The M descriptor defines the presence or absence of more distant metastatic disease.

The method of staging has a major impact on the prognostic implications of the stage classification, a fact that is well recognized by the UICC and AJCC as shown in Table 1. The two most commonly encountered types of stage assessment are *clinical staging* (the stage determined using all information available prior to any treatment) and *pathologic staging* (determined after a resection has been carried out). The extent of clinical staging can vary from a clinical evaluation alone (history and physical examination) to extensive imaging (CT/PET scans) or invasive staging techniques. It must be emphasized that a surgical staging procedure (such as mediastinoscopy) is still part of clinical staging because surgical resection as a treatment has not taken place. Clinical stage is denoted by the prefix "c" and pathologic stage by the prefix "p." The UICC also defines a classification system for the presence or absence of residual tumor after treatment, as shown in Table 2. Typically this is applied to describe the completeness of a surgical resection.

## Development and Methodology of the IASLC Staging System

A proposal to develop an international effort to inform a future revision of the TNM staging classification for lung cancer originated in 1996 at a workshop sponsored by IASLC. An international committee was established and work began in 1999. An unrestricted grant from Eli Lilly and Company enabled the establishment of a database (Eli Lilly and Company played no role in the data collection, analysis, or recommendation development process). The database was developed in cooperation with Cancer Research and Biostatistics (Seattle, WA), which is an independent scientific foundation and the statistical center for the Southwest Oncology Group. Data elements and definitions were finalized in October 2002. Data were collected from multiple sources and sites around the globe. Committees were formed to analyze the data and develop recommendations (including validation and methodology, T, N, M descriptors, nodal chart, prognostic factors, and small cell lung cancer). The initial recommendations were revised and approved by the full IASLC International Staging Committee. These proposals were published in a series of detailed articles in the *Journal of Thoracic Oncology* in 2007.[2–6] The proposed staging recommendations were presented to the AJCC and UICC in 2007, were approved by these bodies, and are slated to be published in the 7th edition of the *UICC Staging Manual* in 2009.

At the time the database was closed to additional entries, 100,869 cases had been submitted from 45 sources in 20 countries.[7] The final data set involved 81,015 cases after exclusion of ineligible cases (due to incomplete information in 42%, outside the 1990 to 2000 time frame in 28%, unknown histology in 13%, incomplete survival data in 6%, recurrent cases in 6%, and ineligible histologic types in 6% [carcinoid, sarcoma, and others]).[5,7] Small cell lung cancer accounted for 16% and NSCLC for 84% of cases. Only the NSCLC cases were used to derive the T, N, M descriptors and stage groupings reviewed in this article. SCLC and carcinoid tumor staging are addressed in separate publications.[8,9] The database included cases from four continents (the proportion of NSCLC cases is as follows: Europe, 58%; North America, 21%; Asia, 14%; and Australia, 7%). Submitted cases came from series (40%), registries (30%), and clinical trials (30%). Treatment involved