

The IASLC lung cancer staging project proposal for the classification of lung cancers with multiple pulmonary sites of involvement: the first step toward finding optimal treatment

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Assessment of multifocal lung tumors and the distinction of synchronous primary tumors from intrapulmonary metastases represent an important problem as this decision significantly influences tumor staging and subsequent treatment strategies. Up to 8% of lung cancer patients present with two or more anatomically separate nodules. Yet, significant variability currently exists in treatments for these patients (1-4). Reasons for such ambiguity are that these patients represent a heterogeneous group of cohorts with marked difference in biological behaviors, survival, and recurrence pattern. Currently, no formal consensus exist among clinicians in terms of staging, treatments, and follow-up.

The article by Detterbeck and colleagues (5) highlights the challenges faced by clinicians in managing lung cancer patients with multiple pulmonary sites involvement and help to clarify the confusion by proposing a modified TNM staging system to incorporate the four different diseases with unique presentation and biological behavior. These recommendations are based on a comprehensive review of relevant articles as well as analyses of the retrospective database of the International Association for the Study of Lung Cancer (IASLC), consisting of more than 77,000 cases of lung cancer diagnosed from 1999 to 2010 (6-8). The article describes four different clinical presentation of lung cancer with multifocal lung involvement: second primary cancer, intrapulmonary metastasis, multifocal lung adenocarcinoma with ground glass/lepidic features, and pneumonic-type lung adenocarcinoma. The tumors are considered second primary tumor if they have clearly a different histology or have a different radiographic appearance, metabolic uptake, growth pattern or different

biomarkers. Each tumor is staged separately based on current TNM staging system. The nodules are considered to be intrapulmonary metastasis if exact matching breakpoints are identified by genetic hybridization or have similar clinical features such as radiographic appearance, growth pattern or significant nodal and systemic metastasis. TNM staging is assigned on the basis of location of the nodule relative to the primary tumor site. If it is in the same lobe, the tumor is designated as T3; if in the same lung (different lobe), as T4; and if in the contralateral lung, as M1a. Tumors are considered multifocal GG/L lung adenocarcinoma if there are multiple subsolid nodules with at least one suspected or proven to be cancer. Ground glass nodule <5 mm or lesion suspected to be AAH is excluded. T stage is based on highest T lesion with (#/m) indicating the multiplicity. Finally, tumor is categorized as a pneumonic-type adenocarcinoma if there is a diffuse pneumonic infiltrate or consolidation with regional distribution; this designation does not apply in case of a single well-demarcated mass causing post obstructive pneumonia or atelectasis or multiple discrete well-demarcated nodules. T stage is based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes.

The proposed classification does have several limitations worth discussing. In an attempt to simplify the classification and to create a common nomenclature to describe clinically different lung cancers with similar appearances, arbitrary lines were drawn to separate the tumors into distinct categories. This arbitration will inherently add subjective bias in categorizing the tumor. Moreover, there will always be cases in borderline zones where the distinct maybe not possible. The reality might be that these entities (e.g.,

multifocal GGN and pneumonic-type adenocarcinoma) exist as a spectrum of disease, rather than discrete entities. Second, the proposal tries to simplify a complex clinical problem by focusing mainly on the T staging for various clinical presentations and does not take account of lymph node involvements; yet the clinical reality is much more complex. Not infrequently, there will be cases where lung nodules in different lobes will present with regional or mediastinal nodal metastasis (e.g., RUL and LLL lung nodules with 4R+ adenocarcinoma). How do we stage this patient then? Also, there will be factors that will obscure the clinical staging of the tumor such infiltrative lung process or nodules related to infection, inflammation. These limitations underscore and highlight the importance of a multi-disciplinary approach and the close cooperation and discussion among different specialists including medical and radiation oncologist, pulmonologists, surgeons, radiologists and pathologists in properly staging and formulating treatment plans.

It is important to note that this proposal is not a recommendation for treatment or management in different clinical presentations. It is a proposal to construct a common nomenclature and classification to different clinically similar yet biologically different lung cancer to allow the majority of patients to be classified more easily and consistently. This effort by the IASLT is an important first step in providing developing guidance toward best “tailored treatment” for these distinct diseases.

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Footnote

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