Who left the PETs out?—Who?—Who?

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Positron emission tomographic (PET) scans and magnetic resonance imaging (MRI) of the brain have had their utility in the staging of lung cancer demonstrated time and again in numerous publications and have been fully integrated into the standard staging algorithms of the National Cancer Center Network, the European Society of Thoracic Surgeons, the American College of Chest Physicians, and a host of others.¹⁻³ But the significantly increasing incidence and evolution of bronchioloalveolar carcinoma—now known as a spectrum from atypical adenomatous hyperplasia, to adenocarcinoma in situ, to minimally invasive adenocarcinoma, and finally to frankly invasive adenocarcinoma (with predominantly a lepidic growth pattern but also acinar and papillary growth patterns)—has begun to challenge the one-size-fits-all approach to the use of PET scans in lung cancer staging.^{4,5} Some surgeons have acknowledged the unique characteristics of radiographic “ground glass” lesions (Figure 1), which exhibit no more than mild PET avidity and signify “noninvasive” adenocarcinomas (atypical adenomatous hyperplasia, adenocarcinoma in situ, and minimally invasive adenocarcinoma). These individuals already have changed their staging practices, whereas others have been more dogmatic. In their article in this issue of the *Journal*, Cho and colleagues⁶ have attempted to document objectively what others have suggested previously; that is, the cancer-specific survival for patients with pure ground glass lesions, particularly those smaller than 3.0 cm, approaches 100%, and this very fact justifies leaving out PET scans in the staging of these lesions. Out of a study population of 211 patients with ground glass lesions, 164 (with 175 lesions) were noted to have “pure” ground glass without a solid (invasive) component. The median size of the lesions was 16.5 ± 6.3 mm (range <10 to >30 mm); pathologic staging

showed T1a (89%) to T3; and treatment ranged from wedge resection (36%) to segmentectomy and lobectomy (61%).

Cho and colleagues compared 136 patients who underwent staging PET and computed tomography with 28 who did not and 109 patients who were evaluated with brain MRIs versus the 55 who were not. No patient had an abnormal brain MRI result, but 3 patients had abnormal PET scan results suggestive of metastatic lymph nodes ($n = 2$) and liver ($n = 1$) lesions. No metastatic lesions were confirmed, however. PET scans thus not only were nearly universally “negative” but in some cases led to additional unnecessary diagnostic testing. In follow-up, all patients who underwent PET or MRI scans had no evidence of metastatic disease; furthermore, patients who were not evaluated with PET or MRI scans also did not have metastatic disease develop. The conclusion of this study was that pure ground glass lung lesions, representing noninvasive adenocarcinoma, have an extremely high cancer-specific survival and do not warrant staging with PET or MRI scans. This finding could also be used to justify the sublobar resections—even wedge resections—used in this group.⁷

Several issues with this study, however, raise caution about the interpretation of the data. First, the patient cohort was relatively small and nonuniform. The International Association for the Study of Lung Cancer staging project demonstrated that large international data sets (ie, 67,725 cases from 46 sources in 19 countries) are much more reliable than small single-institutional cohorts of 164 patients in determining prognostic characteristics.⁸ Second, no patient in the entire group had metastatic disease develop even though 87 invasive adenocarcinomas were included. There were effectively no positive controls. Third, many ground glass lesions are “mixed,” with areas of solid and nonsolid disease, and this study does not address such lesions at all. Finally, the use of wedge resection of lung cancer has always raised suspicion, because by the nature of these procedures lymph nodes are almost never biopsied, and therefore potential lymph node metastases could be missed with inappropriate pathologic tumor downstaging.

In conclusion, Cho and colleagues raise important questions about the extent of staging for noninvasive adenocarcinoma. Certainly, nearly all surgeons will likely agree that brain MRIs are not warranted in this group,

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FIGURE 1. Example of minimally invasive adenocarcinoma as seen with computed tomography (A) and positron emission tomography (B). PET, Positron emission tomography.

although the data are somewhat less convincing regarding PET scans because of the issues raised here. Future staging proposals regarding this patient population will need to include larger data sets and specific recommendations for indications for PET scans as well as MRI in this interesting and important patient population.

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