

## Extending the survival advantage of ground glass

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Comment on: Shin KW, Cho S, Chung JH, *et al.* Comparison of Prognosis of Solid and Part-Solid Node-Negative Adenocarcinoma With the Same Invasive Component Size. *Ann Thorac Surg* 2017;103:1654-60.

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The ground glass opacity (GGO) is a radiographic finding that has become an increasingly informative component of lung adenocarcinomas (1). In 2011, the International Association for the Study of Lung Cancer (IASLC), American Thoracic Society (ATS), and the European Respiratory Society (ERS) proposed a revised classification system for lung adenocarcinoma (2). A major contribution of this system was the parsing of lung adenocarcinomas into prognostic categories based upon the extent of pathologic tumor invasion. In this system, a lepidic growth pattern is described which represent non-invasive growth restricted to neoplastic cells along pre-existing alveolar structures, and this pathologic finding correlates the GGO component on fine-section CT. Reciprocally, invasive tumor histology, represented by a proliferation of invasive tumor cells and collapse of the alveolar wall, correlates with a solid appearance on thin-section CT. In other words, the ground glass components of a part-solid lesion on thin-section CT correspond to the preinvasive components of lung adenocarcinomas on pathologic evaluation, and the solid radiographic components indicate invasive pathology (3-9). The prognostic implications of GGOs have been extensively studied by our Asian colleagues, and these findings have been reproduced and verified in largely non-Asian cohorts (10,11). In general, the greater the extent of radiographic ground glass, the better the overall and recurrence free survival; and the greater the size of the solid component, the worse the overall and recurrence free survival.

These findings have obvious implications for lung cancer staging and have been recognized in the 8<sup>th</sup>

edition American Joint Committee on Cancer's staging system. In this system, the maximum dimension of the solid component (on imaging, c-stage) or the invasive component (on microscopy, p-stage) is used to assign the T category (12). In a recent publication by Shin *et al.* (13), the authors' data highlight the requirement to consider size of the invasive component in the pathologic staging of lung adenocarcinoma. A retrospective analysis of the Seoul National University Bundang Hospital lung cancer database for patients with node-negative lung adenocarcinoma was performed to evaluate the prognosis of pathologically solid adenocarcinomas sized less than 20 mm alongside part-solid adenocarcinomas with an invasive tumor size of less than 20 mm. From 2004 to 2012, 191 patients were categorized either as those with a solid adenocarcinoma consisting only of an invasive component (n=92), or those with part-solid adenocarcinomas consisting of both an *in situ* and invasive component (n=99), and the mean size of the invasive component was similar in both groups (15.9 and 15.2 mm, respectively). Despite the mean total lesion size being larger in the part-solid group (21.0 versus 15.2 mm), 5-year recurrence free survival was statistically improved compared with the solid group (93.7% versus 84.0%). Five-year overall survival was 93.8% in the part solid group, compared to 90.3% in the solid group and this was not statistically different. Lymphovascular invasion and high maximum standardized uptake values (SUV) were significantly more common in the solid group and these two variables were the only independent prognostic factors associated with disease-free survival in multivariate analysis

incorporating all patients in both groups.

Whereas a number of studies have demonstrated that the diameter of the solid component is more accurate in guiding prognosis than total tumor size (10,14), the manuscript by Shin *et al.* take these findings one step further by demonstrating additional insight into tumor biology: despite similar size of invasive components, the addition of an *in situ* (preinvasive) component identifies lung adenocarcinomas with more favorable prognosis. For example, a patient with a 30 mm part-solid adenocarcinoma with a 15 mm solid component would be expected to have a better prognosis than a patient with a 15 mm solid adenocarcinoma. These findings are likely translatable to clinical staging (based on radiographic GGO components), as was suggested by the findings of Tsutani *et al.* These authors observed that the radiographic solid portion size was an independent prognostic factor for disease-free survival in patients with clinical stage IA lung adenocarcinoma, while whole tumor size was not, and importantly these authors also demonstrated that solid tumors have more malignant potential than part-solid tumors even when they have the same sized solid component on CT (9,15). Taken together, these data suggest that the presence of *in situ* carcinoma components pathologically, or ground glass components radiographically, represent lung adenocarcinomas with unique biologic characteristics. Such data drive home the point that not all T1 adenocarcinoma lesions identified on CT are created equal.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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