In recent years, significant attention has been directed toward the radiographic entity of ground glass opacities (GGOs), with regard to their malignant potential and attempts to identify risk of aggressive behavior.1-7 Previous investigators have demonstrated that histologic subtype significantly affects prognosis, with micropapillary and solid lesions associated with worse outcomes.1,2 In addition, a number of authors have attempted to correlate radiographic features with behavior of ground glass lesions.4,6,7 No previous studies, however, have simultaneously attempted to link the combination of imaging characteristics, pathologic subtype, and gene mutation in GGOs. This endeavor was uniquely explored in the article by Sun and colleagues6 in this issue of the Journal.

In this quite timely publication, Sun and colleagues6 present their correlative studies linking selected imaging and histologic characteristics, as well as gene mutations associated with adenocarcinomas arising in GGOs. For this study, patients were divided into 2 groups based on tumor appearance on computed tomography, with Group 1 tumors <2 cm and predominantly ground glass, while Group 2 tumors were larger in size and predominantly solid. Upon comparing pathologic subtype and gene mutations between groups, Sun and colleagues6 found a number of important results that aid us in our understanding of adenocarcinomas arising from GGOs. Aggressive histologic subtypes (micropapillary and solid) were almost entirely found in group 2. In addition, endothelial growth factor receptor (EGFR) mutations were also significantly more likely in group 2. These findings should, of course, be taken in context; while micropapillary and solid histologic features and EGFR mutations were more common in group 2 than in group 1, they still only represented a minority of patients in group 2. Therefore, it’s not as simple as dividing patients into prognostic categories of “high risk” and “low risk;” rather, we can recognize that there are a number of relevant predictors of biologic behavior, but future studies are certainly in need to be able to provide reliable estimates of outcome on a patient-by-patient basis. Overall patterns identified in this study are worth recognizing, as they may prove helpful in determining the ways that we counsel and treat asymptomatic patients with radiographic evidence of larger, predominantly solid GGOs.

In terms of radiographic characteristics, this investigation accounted for only size and solid component; notably absent from the study were such features as pleural tag, air bronchograms, and lobulation, which have been assessed by a number of previous authors.3,7,8 However, this limitation should be deemed a wise choice, rather than an error of omission: in these previous studies, extensive evaluation provided mixed results of questionable utility. Moreover, recent investigations have further shown neither pleural tags, spiculation, nor lobulation to remain relevant after adjusting for the size of the solid component, indicating that those radiographic features are not as important as previously believed.4 Thus, it’s clear that ongoing studies are critical to identify reliable markers associated with favorable tumor biology, and the innovative approach of Sun and colleagues will hopefully guide us as we aim to gauge prognosis and determine optimal treatment strategy.

With regard to extent of treatment, Sun and colleagues6 suggest that their findings may be useful for selecting patients who may benefit from lesser operative procedures,
stating in the perspective statement that “GGOs with a diameter less than 20 mm and a solid component less than 50% are more appropriate for sublobar resection than those with a diameter over 20 mm and a solid component over 50%.” Again, though, a word of caution is in order: extent of resection was not evaluated in this study’s methodology, and additional investigations designed to answer the question of lobectomy versus sublobar resection would certainly be helpful. We are still in our infancy of understanding GGOs, however, and just as it is important to understand how much lung to remove, we are also in need of understanding which GGOs will be adequately managed with alternative modalities (such as ablation or stereotactic radiation), which will require systemic treatment, and which will require no treatment at all.9

References