Correlation between the Size of the Solid Component on Thin-Section CT and the Invasive Component on Pathology in Small Lung Adenocarcinomas Manifesting as Ground-Glass Nodules

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Introduction: We aimed to evaluate the correlation between the size of the solid component on thin-section computed tomography (CT) and invasive component on pathology in small lung adenocarcinomas manifesting as subsolid nodules.

Methods: Fifty-nine subsolid nodules in 58 patients were evaluated. The maximum diameters of subsolid nodules and the solid component on CT were measured by two radiologists in three-dimensional (3D) and two-dimensional (2D) planes using in-house software. In addition, the maximum diameters of the tumor and invasive component were measured on pathology by two pathologists. CT measurements were compared with pathologic measurements.

Results: There was a strong correlation between the size of the solid component on CT and invasive component on pathology, as well as the size of subsolid nodules and the tumor size ($r = 0.82–0.87$ for 3D measurement, $0.72–0.88$ for 2D measurement; $p < 0.0001$). The size of subsolid nodules in 3D and 2D measurements was significantly larger than tumor size ($p < 0.0001$). In regard to measurement of the solid component, 3D measurements tended to be larger than the size of the invasive component whereas 2D measurement tended to be similar to the size of the invasive component. By applying a size criteria of solid component that was 3 mm or lesser in maximum diameter, preinvasive and minimally invasive adenocarcinoma was predicted with a specificity of 100% (28 of 28).

Conclusion: We found a significant correlation between the size of the solid component on thin-section CT and the invasive component on pathology.

Key Words: Subsolid nodule, Lung adenocarcinoma, Minimally invasive adenocarcinoma.

Recently, a new classification of lung adenocarcinomas was proposed by the International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society.1 In this classification, new concepts of adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) were introduced. On the basis of the size of the invasive component and pathologic features, lung adenocarcinomas are now classified into four categories—preinvasive lesions, MIA, invasive adenocarcinoma, and variants of invasive adenocarcinoma. AIS and atypical adenomatous hyperplasia fall under the category of preinvasive lesions for lung adenocarcinoma. With preinvasive lesions and MIA, patients will have 100% or near-100% disease-specific survival, respectively, if completely resected. Furthermore, previously published data have shown that patients with preinvasive lesions or MIA may undergo less extensive surgery such as sublobar resection.2–9 However, to date, it is hard to make a diagnosis of preinvasive lesions or MIA with frozen biopsy specimens, as the invasive component should be precisely evaluated using the entire pathologic sampling. Thus, if preoperative imaging is able to predict the invasive component of adenocarcinomas, it will have great clinical value in determining the extent of surgical resection as well as the patient’s prognosis.

“Subsolid nodule” is a more comprehensive term than “part-solid nodule.” Subsolid nodule refers to both pure ground-glass nodule (GGN) and part-solid GGN, as a category separated from purely solid nodule. Part-solid GGN indicates the nodule that has both ground-glass and solid components.10 In subsolid nodules, many previous reports have demonstrated that ground-glass opacity (GGO)
components represent the lepidic growth and that solid components are frequently related with invasion\textsuperscript{11–23} and also note that computed tomography (CT) plays an important role in the management of subsolid nodules.\textsuperscript{10} It has also been suggested that the T staging in the Tumor Node Metastasis classification should be adjusted radiologically by measuring the solid component of subsolid nodules\textsuperscript{1} and that the management of subsolid nodules should be based on the size of subsolid nodules and the solid component.\textsuperscript{18} The comparison of radiologic–pathologic tumor measurements conducted in several other cancers has demonstrated that radiologic measurement significantly corresponded with pathologic tumor size and may be valuable in treatment planning.\textsuperscript{24–29} To our knowledge, however, no previous study has provided and directly correlated the measurement data between the solid component of subsolid nodules on thin-section CT and the invasive component on pathologic exams.

Therefore, the purpose of our study was to evaluate the correlation between the size of the solid component on thin-section CT and the invasive component on pathology in small lung adenocarcinomas and preinvasive lesions manifesting as subsolid nodules.

**MATERIALS AND METHODS**

This study was approved by the Institutional Review Board of our institution, and written informed consent was waived for all patients in this retrospective study.

**Selection of Cases**

We retrospectively reviewed the medical records of all patients who had undergone surgical resection for small lung adenocarcinomas and preinvasive lesions that manifested as subsolid nodules on CT at our hospital between August 2005 and June 2011. We defined small adenocarcinomas as measuring 3 cm or lesser on the basis of pathologic report. All the tumors had T stage of T1 or lower in our study population. There was a total of 141 eligible patients for whom pathology slides were available. Among them, we excluded 83 patients based on our exclusion criteria defined as follows: (1) time between CT and surgery of more than 4 weeks (n = 11) and (2) patients who were considered to have inappropriate CT images for subsolid nodule analysis (section thickness ≥ 1.25 mm, CT images scanned at outside hospitals or reconstructed with different algorithms; n = 72). Finally, a total of 58 patients (19 men and 39 women) (median age, 61 years; range, 26–85 years) were included in our study. Surgical procedures included wedge resection in 13 patients and lobectomy in 45 patients. The mean time ± standard deviation between CT and surgery was 14.2 ± 12.5 days.

Through the surgical records and transverse CT images, one chest radiologist (JMG) with 21 years of experience reading chest CT images and one radiology resident in her fourth year of training (KHL) identified the location of corresponding subsolid nodules on CT images by consensus. Images were displayed by using a lung window setting with a center of ~700 HU and a width of 1500 HU. When there were multiple subsolid nodules per patient, only subsolid nodules with pathologic confirmation of lung adenocarcinomas were selected based on surgical records. All patients had a single subsolid nodule with pathologic confirmation, except one patient who had two subsolid nodules with pathologic proof. Finally, a total of 59 subsolid nodules were selected in 58 patients for image analysis. The study population and subsolid nodules enrolled in our study partly overlap with those of our previous reports from our department.\textsuperscript{30,31} However, the methodology is totally different from that of prior studies.

**Image Acquisition**

CT images were obtained using one of the following four CT scanners; Sensation 16 (Siemens Medical Solutions, Forchheim, Germany), Somatom Definition (Siemens Medical Solutions, Forchheim, Germany), LightSpeed Ultra (GE Healthcare, Milwaukee, WI), or Brilliance 64 (Philips Medical Systems, Best, The Netherlands). As all data were collected retrospectively, a variety of scanning protocols were used, including CT with (n = 35) or without (n = 23) intravenous contrast material, and CT with standard-dose (n = 45) or low-dose techniques (n = 13). Tube current ranged from 200 to 400 mAs for standard-dose techniques and 20 to 40 mAs for low-dose techniques, with tube voltage of 120 kV for all scans. In all patients, CT images were reconstructed using the high-frequency algorithm with a section thickness of 1.25 mm or 1 mm. The image matrix size ranged from 512 × 512 pixels. The field of view was optimized for the size of the patients and ranged from 300 to 350 mm.

**Assessment of CT Scans**

For the 59 subsolid nodules, two radiologists (Reader 1: a radiology resident (KHL); Reader 2: a chest radiologist (JYW), with 5 years of experience) independently drew the borders of subsolid nodules as well as the solid component and saved them as regions of interest files by using in-house software. On the basis of the regions of interest of subsolid nodules drawn by radiologists for the whole boundary of subsolid nodules and their solid components, the program automatically calculated the maximum diameter in both (three-dimensional) 3D and (two-dimensional) 2D planes and showed the axis of the maximum diameter of subsolid nodules. Two readers then reviewed the measurement results and axes of the maximum diameter generated by the program in all cases and were allowed to adjust the measurements by manually drawing the maximum diameter if the generated results were deemed unacceptable because of long speculations of subsolid nodules in a few cases.

To assess intrareader variability, Reader 1 outlined the boundary of the subsolid nodules as well as the solid component on the CT scans over two sessions (Fig. 1): in the first session, she drew a border around all involved CT sections that contained subsolid nodules to obtain both 3D and 2D measurement data, and in the second session, she only outlined the border of the subsolid nodules and the solid component on the representative CT image with the largest long diameter of subsolid nodules. For cases in which the slice of the maximum dimension of the solid portion was different from that of the maximum dimension of subsolid nodule, she drew a border around the solid component on the slice of...
the largest diameter of the solid portion. There was a 4-week interval between the first and second session. To evaluate interreader variability, Reader 2 drew the boundary of each subsolid nodule and solid component once on a single CT image with the maximum long diameter of subsolid nodules. If multiple separate areas of solid components were present, the border of the largest solid component was outlined. If a large blood vessel was present, the readers attempted not to include the blood vessel.

Pathologic Assessment

All surgical specimens were fixed in an inflated state by means of transpleural and transbronchial infusion of 10% buffered formalin and embedded in paraffin. The specimens were stained with hematoxylin and eosin. For each case, a representative pathologic slide (chosen by HSP, who had 6 years of experience) containing the largest cross-section or representative part of the tumor, was selected. Examined under light microscopy, the borders of the tumor and invasive component were drawn on pathology slides by two pathologists (HSP and HJG, who too had 6 years of clinical experience) in consensus (Fig. 1). Thereafter, all pathology slides were scanned in 1:1 scale along with a transparent millimeter ruler and digitized using a software package (Image-J, version 1.37v, for Windows http://www.ncbi.nlm.nih.gov/). With use of the software, K.H.L. manually redrew the tumor borders along the indicators that the pathologists had marked on pathology slides and measured the maximum diameter of the tumor and invasive component. The final pathologic diagnoses were determined postoperatively by a retrospective pathologic review of all specimens by the two pathologists, according to the new adenocarcinoma classification.

Exploratory Analysis

We conducted additional exploratory analyses and evaluated the specificity and sensitivity of CT measurements in predicting preinvasive and MIA lesions.

Statistical Analysis

For comparison, the mean measurements of subsolid nodules and solid components were used. Measurement data on CT was compared with the pathologic reference diameter using the paired \( t \) test (a parametric test was used because data were observed to be normally distributed) and Pearson’s correlation test.

Interreader variability and intrareader variability for the measurements on CT were analyzed by calculating the intra-class correlation coefficient (ICC) (0–0.20, poor correlation; 0.21–0.40, fair correlation; 0.41–0.60, moderate correlation; 0.61–0.80, good correlation; and 0.81–1.00, excellent correlation) and 95% Bland-Altman limits of agreement. The one-way analysis of variance test was used to compare the measurement data on CT according to lung adenocarcinoma categorization. All statistical analysis was performed using two commercially available software programs (SPSS 18.0 for Windows, SPSS, Chicago, IL, and MedCalc 12.1.4.0, MedCalc Software, Mariakerke, Belgium). For all studies, a difference with a \( p \) value of less than 0.05 was considered statistically significant.

FIGURE 1. A and B, Axial computed tomography image showing a peripheral ground-glass opacity and a central area of increased attenuation. Readers manually outlined the subsolid nodule (yellowish green) and its solid component (yellow), which was used to calculate the maximum diameter. C and D, A digitized image of the representative pathologic slide revealed that this part-solid GGN was an invasive adenocarcinoma. The border of the overall tumor (marked by blue dots) and the invasive component (marked by red dots) was manually drawn by two pathologists in consensus. (Hematoxylin–eosin stain; original magnification in (C) ×1.0; and (D) ×40.) GGN, ground-glass nodule; ADC, adenocarcinoma.
RESULTS

Nodule Characteristics
Of 59 subsolid nodules, 44 cases were part-solid GGNs and 15 were pure GGNs on CT. Pathologic exam revealed 16 preinvasive lesions (3 atypical adenomatous hyperplasia and 13 AIS), 15 MIA, and 28 invasive adenocarcinomas. The means tumor size ± standard deviations described in the pathologic reports were 8.9 mm ± 4.2 in preinvasive lesions, 13.4 mm ± 3.4 in MIA, and 16.9 mm ± 4.6 in invasive adenocarcinomas.

CT and Pathology Measurement
The maximum diameter of subsolid nodules and the solid component in the 3D plane is abbreviated as 3D Nodule and 3D Solid. On axial CT images with the maximum diameter of subsolid nodules, the size of subsolid nodules and the solid component was measured and is shown as 2D Nodule and 2D Solid. 2D Solid largest represents the maximum diameter of the solid component on axial CT images regardless of the size of subsolid nodules. The relationship between CT and pathologic measurements is presented in Table 1. A significant correlation was noted in the maximum diameter of subsolid nodules on CT and tumor size on pathology (r = 0.82 for 3D measurement, 0.81–0.82 for 2D measurement; p < 0.0001). Moreover, there was a significant correlation in maximum diameter between the solid component on CT and the invasive component on pathology (r = 0.87 for 3D measurement, 0.72–0.88 for 2D measurement; p < 0.0001). The strongest correlation was obtained for 2D Solid largest measurement (r = 0.88).

In this study, CT images showed a tendency to display the tumor size in its larger diameter on both 3D and 2D measurements. For tumor size measurements, differences in maximum diameter between CT and pathology measurements were significant (mean difference, 10.38 mm for 3D; 4.93–6.05 mm for 2D; p < 0.0001). With regard to solid component measurement, 3D measurements tended to overestimate the invasive component whereas 2D measurements tended to display the invasive component in a similar diameter. For the solid component, the difference in maximum diameter between 3D CT and pathology measurements was significant (mean difference, 4.23 mm for 3D measurement, p < 0.0001). With 2D measurements, there were no significant differences between the pathology measurements for 2D Solid largest measurement during the second session by Reader 1 (mean difference −0.22 mm) and 2D Solid measurement (−0.18 mm) by Reader 2 (p > 0.05). However, significant differences were noted for 2D Solid (mean difference, −1.28 mm, p = 0.02), 2D Solid largest (1.21 mm, p = 0.003) during the first session, and 2D solid (−1.42 mm, p = 0.02) during the second session by Reader 1.

Interreader and Intrareader Variability
Both interreader and intrareader agreements in CT measurements were excellent (ICC range, 0.92–0.98). Bland-Altman plots with 95% limits of agreement are shown in Figs. 2 and 3. In general, scatter of measurement differences around the mean was independent of tumor diameter.

Lung Adenocarcinoma Categorization
Of the 15 MIA cases, 10 cases were part-solid GGNs and five were pure GGNs on CT. The mean size of the solid component in MIAs was 4.9 mm (range, 0–9.6 mm), 2.4 mm (0–8.0 mm), and 3.6 mm (0–7.8 mm) on 3D Solid, 2D Solid, and 2D Solid largest measurements, respectively. In five MIA cases manifesting as pure GGNs, the size of the invasive component was 1.4, 1.4, 3.0, 3.4, and 4.3 mm on pathology.

TABLE 1. Mean Difference and Correlation Coefficient for Measured Diameters on CT and Pathology

<table>
<thead>
<tr>
<th>Reader and Measurement Variable</th>
<th>Mean Measurement Difference (mm) = CT Diameters Minus Pathology Diameters</th>
<th>p Value</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader 1_1st session</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D Nodule</td>
<td>10.38 (8.95, 11.81)</td>
<td>&lt;0.0001</td>
<td>0.82</td>
</tr>
<tr>
<td>2D Nodule</td>
<td>6.05 (5.05, 7.05)</td>
<td>&lt;0.0001</td>
<td>0.82</td>
</tr>
<tr>
<td>3D Solid</td>
<td>4.23 (2.99, 5.47)</td>
<td>&lt;0.0001</td>
<td>0.87</td>
</tr>
<tr>
<td>2D Solid</td>
<td>−1.28 (−2.36, −0.20)</td>
<td>0.02c</td>
<td>0.77</td>
</tr>
<tr>
<td>2D Solid largest</td>
<td>1.21 (0.42, 1.99)</td>
<td>0.003c</td>
<td>0.88</td>
</tr>
<tr>
<td>Reader 1_2nd session</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D Nodule</td>
<td>4.93 (3.98, 5.87)</td>
<td>&lt;0.0001</td>
<td>0.81</td>
</tr>
<tr>
<td>2D Solid</td>
<td>−1.42 (−2.58, −0.26)</td>
<td>0.02c</td>
<td>0.74</td>
</tr>
<tr>
<td>2D Solid largest</td>
<td>−0.22 (−1.23, 0.79)</td>
<td>0.67</td>
<td>0.8</td>
</tr>
<tr>
<td>Reader 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2D Nodule</td>
<td>5.69 (4.63, 6.75)</td>
<td>&lt;0.0001</td>
<td>0.81</td>
</tr>
<tr>
<td>2D Solid</td>
<td>−0.18 (−1.42, 1.05)</td>
<td>0.77</td>
<td>0.72</td>
</tr>
</tbody>
</table>

aThe maximum diameter of subsolid nodules and solid component in 3D plane is abbreviated to 3D Nodule and 3D Solid. 2D Nodule and 2D Solid represents the size of subsolid nodule and solid component on axial CT image with the maximum diameter of subsolid nodule. 2D Solid largest represents the maximum diameter of solid component on axial CT image, regardless of the size of subsolid nodule.

bNumbers in parentheses are the 95% confidence interval.

cPaired t test.

dSignificant difference.
To identify useful CT measurements in predicting preinvasive lesions or MIAs, we compared the CT measurements of the preinvasive, MIA, and invasive adenocarcinoma groups (Table 2). All pure GGNs were confirmed as either preinvasive lesions (67%, 10 of 15) or MIAs (33%, 5 of 15). In the invasive adenocarcinoma group, all lesions included a solid portion and presented as part-solid GGNs. With regard to CT measurements, all measurements showed significant differences among the three groups ($p < 0.0001$). On subgroup analysis, the invasive adenocarcinoma group showed a larger size of subsolid nodules, solid component, and a higher size ratio of solid component to subsolid nodules than the preinvasive lesion and MIA groups. There were no significant differences in CT measurements between the preinvasive lesion and MIA groups ($p > 0.05$).

**Radiologic Measurement in Predicting Preinvasive and MIA Lesions**

Additional exploratory analysis was performed to determine 2D CT measurement values useful in predicting preinvasive and MIA lesions with high specificity (Table 3). The highest specificity of 100% (28 of 28) was observed with a size criteria of Solid$_{\text{largest}}$ of 3 mm or lesser. All the invasive lung adenocarcinomas included the solid portion larger than 3 mm in largest diameter. When a size criteria of Solid$_{\text{largest}}$ of 5 mm or lesser was applied, three invasive lung adenocarcinomas were categorized under the radiologic preinvasive and MIA groups, resulting in a specificity of 89% (25 of 28). We also examined the measurement criteria that was previously suggested by Suzuki et al.$^{11}$ When the criteria of subsolid nodules of 20 mm or lesser with a solid component of 0.25 or lesser to the maximum diameter of subsolid nodule was applied, it also showed 100% specificity (28 of 28) in predicting preinvasive and MIA lesions.

**DISCUSSION**

In this retrospective study, we correlated the CT and pathologic measurements of small adenocarcinomas manifesting as subsolid nodules, and investigated the CT measurements according to the lung adenocarcinoma categorization. The main findings of this study are: (1) The size of subsolid nodules and solid components on CT significantly correlated with that of the tumor and invasive component on pathology in small lung adenocarcinomas; (2) 3D measurements of the size of the solid component showed a tendency to be larger than the size of the invasive component, whereas 2D measurements tended to be similar to the size of the invasive component; and (3) A size criteria of Solid$_{\text{largest}}$ 3 mm or lesser may predict preinvasive and MIA lesions with high specificity.

For the differences between CT and pathology measurements observed in our data, there are several possible explanations. First, in addition to thevariability of CT measurements values in predicting preinvasive and MIA lesions with high specificity ($p > 0.05$). We also examined the measurement criteria that was previously suggested by Suzuki et al.$^{11}$ When the criteria of subsolid nodules of 20 mm or lesser with a solid component of 0.25 or lesser to the maximum diameter of subsolid nodule was applied, it also showed 100% specificity (28 of 28) in predicting preinvasive and MIA lesions.

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size of the invasive component. However, even though some CT measurements showed significant differences from pathology measurements because of the reasons described above, our results demonstrated that the correlation between CT and pathology measurements were significant.

Until now, there has been very little research conducted to correlate radiologic and pathologic measurements in lung adenocarcinoma. Our data are consistent with previous reports in that CT measurements tended to overestimate the true pathologic size of the tumors with a significant difference. Furthermore, in this study, 3D solid CT measurements also showed a tendency to overestimate the invasive component, whereas 2D solid CT measurements tended to be similar to the size of the invasive component. To date, however, the optimal window setting for assessing tumor size or the invasive component has not been clarified. Therefore, with our study population, we examined new window settings for the optimal evaluation of subsolid nodules and solid components on thin-section CT (Appendices 1-3, Supplementary Digital Content 1, http://links.lww.com/JTO/A520). In the evaluation of subsolid nodule size, GGN setting 1 (−520, 1) was the most accurate in determining the pathology tumor size. Because of the wide variety of CT attenuation values of GGOs and the lower contrast of GGOs against the surrounding pulmonary parenchyma compared with the solid portion, setting a fixed CT attenuation cutoff value for the subsolid nodule boundary may have contributed to a more precise measurement. Further studies are needed to validate the clinical application of this window setting. In the estimation of the solid component, we found that the size of the solid component displayed at the lung window setting (LWS; −700, 1500) better correlated with that of the invasive component than other window settings. Thus, when assessing the size of the solid portion in part-solid GGNs, we believe that LWS (−700, 1500) itself may

FIGURE 3. Bland-Altman plots showing intrareader agreement of two-dimensional size measurements for subsolid nodules (A), solid component (B), and solid largest (C). X axes show mean measurements and y axes show differences between measurements of the two reading sessions by Reader 1. Solid lines = mean absolute differences. Dashed lines = 95% limits of agreement. GGN, ground-glass nodule.
be sufficient to predict the size of the invasive component on pathology. There have been attempts to separate preinvasive adenocarcinoma from invasive carcinoma by measuring tumor dimensions on CT. Suzuki et al.11 reported that lung carcinoma that was 2.0 cm or lesser in size and with a consolidation of 25% of lesser of the maximum tumor diameter was considered to be radiological early lung cancer. In pure GGNs, 8 mm and 10 mm have been suggested as thresholds that showed high specificity in differentiating premalignant lesions from malignant lesions and preinvasive lesions from invasive adenocarcinomas, respectively.10,11 However, CT findings or measurement thresholds for MIAs have not been reported. In our study, MIA appeared as pure GGNs in one third of cases (5 of 15) and presented as part-solid GGNs consisting of a predominant GGO component and a small central solid component in two thirds of cases (10 of 15). On quantitative analysis, our data showed that there was no significant difference in the maximum diameter of subsolid nodules and the solid component between MIAs and preinvasive lesions. On the contrary, invasive lesions showed significantly larger subsolid nodule size and solid component than preinvasive and MIA lesions. On the basis of these different imaging characteristics, we believe that thin-section CT may be able to predict preinvasive and MIA lesions preoperatively, so as to determine the eligibility of patients for limited surgical resection. To avoid patients undergoing limited resection for invasive adenocarcinomas, specificity was considered the most important factor. Both of a size criteria of solid largest 3 mm or lesser and the measurement criteria previously suggested by Suzuki et al.,11 subsolid nodules that were 20 mm or lesser with a solid component of 0.25 or lesser to the maximum diameter, showed 100% specificity. As measuring the size of the solid component in largest diameter is a more convenient and simpler way than measuring and calculating the ratio of two variables, we suggest that a size criteria of Solid largest of 3 mm or lesser may be a safe and useful radiologic measurement in predicting preinvasive and MIA lesions preoperatively with high specificity. We anticipate that the diagnostic accuracy of these radiologic measurements as well as the precise role of

### TABLE 2. CT Measurement Comparison between Preinvasive, MIA, and Invasive Groups

<table>
<thead>
<tr>
<th>Subsolid nodule classification</th>
<th>Preinvasive (n=16)</th>
<th>MIA (n=15)</th>
<th>Invasive (n=28)</th>
<th>p Valuea</th>
<th>Preinvasive vs. MIA</th>
<th>Preinvasive vs. Invasive</th>
<th>MIA vs. Invasive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pure GGNs, no. (%)</td>
<td>10 (63%)</td>
<td>5 (33%)</td>
<td>0 (0%)</td>
<td>&lt;0.0001</td>
<td>0.16</td>
<td>&lt;0.0001</td>
<td>0.003</td>
</tr>
<tr>
<td>Pure-solid GGNs, no. (%)</td>
<td>6 (37%)</td>
<td>10 (67%)</td>
<td>28 (100%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT diameter (mm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3D Nodule</td>
<td>5.2–26.7 (15.8±6.9)</td>
<td>11.1–30.6 (20.9±5.4)</td>
<td>16.0–45.1 (29.2±7.2)</td>
<td>&lt;0.0001</td>
<td>0.07</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3D Solid</td>
<td>0–12.1 (2.5±3.8)</td>
<td>0–9.6 (4.9±4.0)</td>
<td>8.8–30.6 (18.6±6.3)</td>
<td>&lt;0.0001</td>
<td>0.08</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3D Solid/Nodule</td>
<td>0–0.59 (0.16±0.23)</td>
<td>0–0.46 (0.23±0.18)</td>
<td>0.28–0.96 (0.64±0.16)</td>
<td>&lt;0.0001</td>
<td>0.38</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2D Nodule</td>
<td>4.6–24.5 (12.8±5.4)</td>
<td>9.4–25.2 (17.3±5.2)</td>
<td>13.2–32.1 (22.6±4.7)</td>
<td>&lt;0.0001</td>
<td>0.014</td>
<td>&lt;0.0001</td>
<td>0.004</td>
</tr>
<tr>
<td>2D Solid</td>
<td>0–6.0 (1.5±2.0)</td>
<td>0–8.0 (2.4±3.1)</td>
<td>0–20.9 (9.5±6.0)</td>
<td>&lt;0.0001</td>
<td>0.51</td>
<td>&lt;0.0001</td>
<td>0.0002</td>
</tr>
<tr>
<td>2D Solid/Nodule</td>
<td>0–0.54 (0.12±0.16)</td>
<td>0–0.55 (0.13±0.17)</td>
<td>0–0.80 (0.41±0.23)</td>
<td>0.0001</td>
<td>0.84</td>
<td>0.0002</td>
<td>0.0005</td>
</tr>
<tr>
<td>2D Solidlargest</td>
<td>0–7.3 (1.6±2.5)</td>
<td>0–7.8 (3.6±3.0)</td>
<td>3.7–21.2 (11.9±4.9)</td>
<td>&lt;0.0001</td>
<td>0.06</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2D Solidlargest/Nodule</td>
<td>0–0.57 (0.13±0.20)</td>
<td>0–0.53 (0.21±0.17)</td>
<td>0.22–0.83 (0.52±0.17)</td>
<td>&lt;0.0001</td>
<td>0.3</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Unless otherwise specified, data are range (mean values ± standard deviations). Three-dimensional and 2D Solid/Nodule is the ratio of the maximum diameter of solid component to that of subsolid nodules in 3D plane and 2D plane, respectively.

aCalculated using the χ² test in comparing the adenocarcinoma classification and the one-way analysis of variance test in comparing CT diameter.

bCalculated using Tukey post hoc comparison tests.

CT, computed tomography; 2D, two-dimensional; 3D, three-dimensional; MIA, minimally invasive adenocarcinoma.

### TABLE 3. Diagnostic Accuracy of the Two-Dimensional Measurement Criteria in Predicting Pathological Preinvasive and MIA Lesions

<table>
<thead>
<tr>
<th>Solidlargest ≤ 5 mm</th>
<th>Solidlargest ≤ 3 mm</th>
<th>Subsolid Nodule ≤ 20 mm with ≤ 0.25 Solid Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>61% (19/31, 95% CI: 47–73)</td>
<td>42% (13/31, 95% CI: 25–61)</td>
</tr>
<tr>
<td>Specificity</td>
<td>89% (25/28, 95% CI: 78–96)</td>
<td>100% (28/28, 95% CI: 88–100)</td>
</tr>
<tr>
<td>PPV</td>
<td>88% (23/26, 95% CI: 77–95)</td>
<td>100% (13/13, 95% CI: 75–100)</td>
</tr>
<tr>
<td>NPV</td>
<td>76% (25/33, 95% CI: 63–86)</td>
<td>61% (28/46, 95% CI: 46–75)</td>
</tr>
</tbody>
</table>

Numbers in parentheses are numerators/denominators, 95% CI.

CI, confidence interval; MIA, minimally invasive adenocarcinoma; PPV, positive predictive value; NPV, negative predictive value. 
limited resection may be better confirmed in future randomized prospective trials.

There are some limitations to our study. First, as our patient evaluation was retrospective, there was unavoidable selection bias. Second, a relatively small number of patients were evaluated in this study. Third, we used a single representative pathology slide for each case, which was not sectioned in the same axial plane of CT scans, limiting accuracy in correlating CT and pathology measurements. However, this was unavoidable in our study, as pathologists had not thoroughly measured the size of the invasive component during routine clinical practice before the concept of MIA had emerged. To overcome this limitation, we obtained various CT measurements, including both 3D and 2D. We believe that this limitation can be overcome in a further prospective study, in which pathologic specimens are consecutively sectioned in the same transaxial plane as the CT scan.

In conclusion, we found a significant correlation between the size of the solid component on thin-section CT and the invasive component on pathology in small lung adenocarcinomas manifesting as subsolid nodules.

REFERENCES

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