Peer Review File
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Reviewer A

This is an interesting article about the underestimation of tumour size in patients with honeycombing. I believe that some modifications can be made in order to improve the article.

Comment 1: As the authors point out, collimation and reconstruction thickness are important factors in determining the size of a pulmonary nodule. I believe that the percentage of patients with thicknesses less than 2 mm and those with thicknesses greater than 5 mm should be evaluated and assessed whether there are differences that may be due to it. On the other hand, despite the absence of significant differences, up to 33% of patients with honeycombing were analyzed only with images in the axial plane (a higher percentage than in the rest of the entities).
Reply 1-1: Thank you very much for your appropriate suggestion. We divided the subjects into two groups of patients whose tumors were assessed by imaging planes with slice width ≦2mm (n=786) and ≧5mm (n=55) and assessed the incidence of preoperative radiological tumor size underestimation in each group. As a result, the incidences of tumor size underestimation in two groups were comparable (≦2mm versus ≧5mm, 64/786 [8.1%] versus 3/55 [5.5%], no statistically significant difference).
Changes in the text 1-1: We added the result of this analysis and its interpretation in the discussion section in the revised manuscript (see Page 15, lines 329-336).

Reply 1-2: In addition, as the reviewer pointed out, we suspected at the beginning of this study that analysis only with images in the axial plane could have been the risk of radiological tumor size underestimation. However, as shown in Table 3, the proportions of the axial plane (versus MPR) utilized for the analysis of tumor size in the patients with and without tumor size underestimation were comparable (14.4% versus 10.1%, no statistically significant difference). Moreover, multivariate analysis revealed that the imaging plane (only axial plane versus MPR) was not a predictor for tumor size underestimation in this study. On the other hand, as the reviewer indicated, up to thirty-three percent of patients with honeycombing were analyzed only with images in the axial plan, whereas only 13.3%, 15.0%, and 13.4% of patients with reticulation, emphysema, and normal parenchyma were analyzed with the axial images. It might has caused higher incidence of tumor size underestimation in the patients with honeycombing than in those with other findings.
Changes in the text 1-2: We added the discussion of this issue in the paragraph of study limitations (see Page 15-16, lines 337-348).

Comment 2: -On the other hand, it would be important to know to what the authors

attribute the underestimation in cases of normal parenchyma. It is understandable that there are differences in patients with honeycombing, but this should also be explained in patients with normal lung.
Reply 2: Thank you very much for your suggestive comment. To answer this suggestion, we divided 628 subjects with normal parenchyma adjacent to the tumor into ones with (n=47) and without (n=581) tumor size underestimation and performed univariate analysis of several risk factors. Pleural invasion of the tumor was significantly more frequent in the patients with tumor size underestimation (12/47 [25.5%]) than in those without underestimation (66/581 [11.4%]) (p=0.01). We examined histopathology of several cases with pleural invasion of the tumor and found that pleural invasion itself did not lead to cause an underestimation of tumor size. The tumors with pleural invasion in the patients with normal parenchyma (n=78) showed significantly larger radiological and pathological tumor sizes than those without pleural invasion(n=550) (radiological, 32.4±15.8 versus 22.9±13.4mm, p<0.001; pathological, 30.9±15.1 versus 21.1±13.1mm, p<0.001). At the same time, the patients with tumor size underestimation had significantly larger radiological and pathological tumor sizes than did those without tumor size underestimation (radiological, 29.9±14.2 versus 23.6±13.9mm, p<0.001; pathological, 47.4±16.4 versus 20.3±11.3mm, p<0.001). It has been reported that larger tumor size was a risk for radiological tumor size underestimation probably due to difficulties in obtaining the largest cross section of tumors on the CT images (reference [16]). Moreover, in other underestimated cases, tumors sometimes extended into narrow lung parenchyma parallel to relatively large sized broncho-pulmonary arterial bundle or into lymphatic vessels along interlobular septum or beneath the pleura, which were not usually visualized on the CT images.
Changes in the text: We discussed this issue in the discussion section (see Page 13-14, lines 285-306).

Comment 3: -In the discussion section, I would indicate that underestimation is also important in non-surgical patients since it affects the prognosis of the disease.
Reply 3: We agree with the reviewer's opinion.
Changes in the text: We added the sentence "radiological tumor size underestimation is also important in patients who do not undergo surgery since it could affect the prediction of the patients' prognosis" in the discussion section (see Page 14-15, lines 318-320).

Reviewer B

Overall, interesting retrospective observational study providing useful insights into an area not well studied.

Comment 1: -are there other studies/data for underestimation of tumor size on ct chest imaging vs pathologic without chronic lung disease (for comparison)?
Response 1: Thank you very much for your constructive suggestion.

Fukui et al. reported that maximum tumor dimension was underestimated (defined as 10 mm or more in pathological tumor dimension compared with radiological ones by preoperative computed axial tomography) in 3.2% of patients without IIPs (reference [5]). Park et al. compared maximal tumor diameters between fresh pathology specimens and CT images in lung adenocarcinoma and found that postoperative up-staging occurred in 12.3% and 1.4% of tumors on performing radiological staging using axial and multiplanar reformatted CT images (reference [17]).
Changes in the text: We added the manuscript written by Park, et al. as reference number 17 (see Page 20, lines 444-446) and supplied the above information in the discussion section (see Page 12, lines 264-270).

Comment 2: - table 1 - consider removing p-values unless it was a pre-specified comparison
Response 2: Thank you for your appropriate suggestion.
Changes in the table: We removed *p*-values from Table 1 according to the reviewer's suggestion (see Table 1).

Comment 3: - the sample size for those with HC is fairly small - a larger sample size would make the association more robust
Response 3: We agree with the reviewer's opinion. However, we could collect only 15 patients with honeycombing adjacent to the tumor during the period of 5 and a half years. To collect larger number of samples, we have to do multicenter study. We would like to plan it as our future project.
Changes in the text: We added some sentences regarding this issue in the study limitation paragraph of the discussion section (see Page 15, lines 325-327).

Reviewer C

Comment 1: Table 1: The label "CT images" is not self explaining, please provide information about the meaning. The same is true for table 3.
Response 1: Thank you very much for your appropriate suggestion.
Changes in the table: We corrected the labels "CT images" to "Imaging plane" and "Axial" to "Axial plane" (see Tables 1 and 3). In addition, we added the explanation of an abbreviation, MPR, in the footnotes of Tables 1 and 3 (see Tables 1 and 3).

Comment 2: Figure 2: Basically, the complete IIP area was infiltrated by the tumor. Please provide at least one more example showing a classical honeycombing lung with a tumor.
Response 2: Thank you for your suggestion.
Changes in the text and Figures: We added one more case example with adenocarcinoma extending to fibrotic lung tissue adjacent to honeycomb lung as advised (see Page 9-10, lines 193-206; Figure 2D-F; and Figure legends of Figure 2).