

Peer Review File

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Reviewer A

My comments are as follows.

1. Did you perform lymph nodes sampling for staging? Please clarify in Methods.

Comment 1: Did you perform lymph nodes sampling for staging? Please clarify in Methods.

Reply 1: sampling of lymph node is not a routine procedure. Only significant evidence of invasiveness in apparent, we perform anatomical resection with lymph node sampling.

Changes in the text: we have modified our text as advised (see Page 6 line 126)

2. In Page 12 Line 252, what is GGB?

Comment 2: In Page 12 Line 252, what is GGB?

Reply 2: I am sorry to this literal. It is GGN.

Changes in the text: I changed GGB to GGN in page 12 line 252.

3. Information of Figure 4 and Table 3 are the same, so that you may delete Figure 4.

Comment 3: Information of Figure 4 and Table 3 are the same, so that you may delete Figure 4.

Reply 3: thank you for your kind comments. We removed figure 4.

Changes in the text: we removed figure 4 and change description (see page 11 line 223)

4. To show the usefulness of the newly proposed CT parameter, you need examine multivariate analysis with cutoff value of 5.41 in -300 HU of

Comment 4: To show the usefulness of the newly proposed CT parameter, you need examine multivariate analysis with cutoff value of 5.41 in -300 HU of

Reply 4: We are proposing a single variable which is the proportion of GGN volume higher than -300 HU. The newly proposed variable gives sensitivity of 85% and specificity of 95% as a result at the cut off value of 5.41. However, as reviewer suggested combining proposed parameter with other well-known CT parameters and apply multivariate analysis will certainly give better result and should be done as a future work.

Changes in the text: we don't change the text.

Reviewer B

The point of view in the study is not particularly novel.

Case number is too small to make a solid conclusion.

Furthermore, it is difficult to understand the result that half of pure GGNs were diagnosed as invasive adenocarcinomas.

There is too large a discrepancy in imaging or pathology diagnosis.

In this type of study, validation work with another cohort is also a good way to gain credibility.

Reply 5:

Thank you for your critical feedback. We acknowledge that the sample size in our study is small and that larger, multicenter studies are needed to validate our findings. It is hard to getting large number of small pure GGN correlates with pathologic diagnosis. We are currently in the process of planning such a study and hope to be able to report more definitive result in the future to you. Regarding the discrepancy between imaging and pathology diagnoses, we agree that this is an important issue to address. All GGNs were diagnosed by experience pathologist who working for lung cancer for 30 years long. However, it is strange that some pure GGN lesions diagnosed as invasive adenocarcinoma and it is the starting point of this study. We appreciate your suggestion to consider validation work and will conduct validation work with international multicenter cohort.

Changes in the text: we don't change the text.

Reviewer C

The weakness of this paper is the small number of cases and the lack of comparison with prognosis; Kamiya et al. reported that volume >0HU correlates with postoperative recurrence of GGN (Radiology 2018 PMID: 29533722).

The description of CT scan is insufficient and should be described in more detail because CT values vary depending on imaging and reconstruction parameters (mAs, kV, rotation speed, reconstruction kernel, etc) .

What CT scanner was used?

Reply 6: Our institution use Siemens SOMATOM Definition Flash CT scanner.

Was contrast medium used?

Reply 7: contrast medium was not used for navigation bronchoscopy.

Changes in the text: we add name of CT scanner and usage of contrast media in methods (see page 7 line 139-140)