

Peer Review File

Article information: <https://dx.doi.org/10.21037/ccts-21-36>

Reviewer #1

This article provides a nice practical summary of radiologist's role in the acquisition of tissue biopsy from small pulmonary nodules. The article is important, but somewhat chaotic and does not read well.

We thank Review #1 for the constructive suggestions. We have applied the suggested modifications as described below.

Comment 1: The diagnostic accuracy of the biopsy for example should be discussed in more detail according to nodule diameter, whereas the molecular testing should be shortened as it is not the key part of the evaluation of small nodules as the title indicates – most of these patients will be treated by surgery and probably never be treated with targeted therapies, as opposed to advanced lung cancer patients. It is also important to know when the text concerns the FNA or core-needle biopsy.

Based on the suggestions from Reviewer #1 and #2, the Biomarker section has been drastically shortened due to its limited applicability to this topic. A more recent reference has also been provided. We have also expanded the Diagnostic Accuracy section in response to comments from both reviewers. We now discuss the effect of various factors on diagnostic accuracy.

Please consider specific comments below:

Comment 2: Page 2 Lung biopsy in CT screening

The information about the Screening program name you refer to should be mentioned in the text.

We have applied the suggested modification.

Comment 3: Bottom of page 4: When discussing "lower incidence of pneumothorax" please use the terminology that is associated with statistical significance - meaning that if there is no difference according to P value, it is prudent to say "similar incidence of ..."

We have applied the suggested modification.

Comment 4: Page 6: Please provide details of the incidence of pneumothorax according to ref. 41, the above comment on "lower rate" but "not statistically significant" applies here.

We have applied the suggested modification.

Comment 5: Page 6. Please discuss briefly the management of rare but important complications, such as air embolism.

We have applied the suggested modification.

Comment 6: Page 8: The chapter on biomarkers for personalized medicine is too lengthy and outdated. This manuscript deals with small nodules, for which there is generally no need to perform extensive biomarker testing, as most of the malignant tumors will be operated on anyway and no targeted treatments are used in these patients. Please be concise, refer to the table, and update this chapter for new targets such as BRAF, KRAS G12C, etc. Also, please clearly indicate if FNA is sufficient for molecular testing of core-needle biopsy is needed.

Based on the suggestions from Reviewer #1 and #2, the Biomarker section has been drastically shortened due to its limited applicability to this topic. A more recent reference has also been provided.

Ideal needle type for molecular analysis is described under the Biopsy Planning section, with references provided.

Comment 7: Page 8 line 5: The prevalence of EGFR mutations in the Western population is between 10-15%, not 20%, and up to 50% in the Far East.

We have applied the suggested modification.

Comment 8: Page 8 line 13: VEGF is not a predictive marker for bevacizumab treatment - please delete this sentence.

We have applied the suggested modification.

Comment 9: Page 10: Conclusion statement should be more informative and more in line with presented data and title, rather than obvious statement.

We have applied the suggested modification.

Comment 10: Fig. 3a: Please erase the text from the scan for clarity.

The text cannot be erased as the original CT DICOM file is no longer available. The text can be photoshopped out by the graphics team if allowed by the publisher and if necessary.

Reviewer #2

This article reviewed and gave a comprehensively summarize the role of CT-guided biopsy in pulmonary lesions from many aspects. The article is of great value, but the article should be more closely related to the topic or title, cutting out extraneous chapters and adding some details related to the topic. The authors should consider the following comments:

We thank Review #2 for the constructive suggestions. We have applied the suggested modifications as described below.

Comment 1: The purpose of this paper is to explore the diagnosis of “small lung nodules”, and the most important problem to be solved in this part of patients is to avoid false negative and to improve the accuracy of diagnosis, rather than the diagnosis of the particular biomarkers. After all, the primary treatment for pulmonary nodules is surgery or stereotactic radiotherapy, not targeted therapy or immunotherapy. Therefore, the chapter of “Diagnostic accuracy” should be discussed in much more detail, such as the size of the nodule, the type of the nodule (solid or part-solid, with or without cavity), the position of the nodule and whether the nodule has increased FDG-F18 uptake, etc.

Based on the suggestions from Reviewer #1 and #2, the Biomarker section has been drastically shortened due to its limited applicability to this topic. A more recent reference has also been provided. We have also expanded the Diagnostic Accuracy section in response to comments from both reviewers. We now discuss the effect of various factors on diagnostic accuracy.

Comment 2: The title of this paper is to explore the role of radiologist in the diagnosis of pulmonary diseases. The radiological diagnosis methods in pulmonary nodules are not limited to CT-guided lung biopsy. For example, it has been recently reported that the diagnostic rate of PET-CT guided lung FNA is better than that of CT-guided FNA.

PET-CT guided lung biopsy is not performed in real-time. CT-guided biopsy is performed in real-time, utilizing a prior PET-CT as a reference (if available), and is the definition of PET-CT guided biopsy. In other words, Chest CT and PET-CT (when available) are reviewed prior to every CT-guided biopsy as the standard of care.

Comment 3: The chapter on Biomarker needs to be streamlined and the literature updated.

Based on the suggestions from Reviewer #1 and #2, the Biomarker section has been drastically shortened due to its limited applicability to this topic of small lung nodules.

Comment 4: Content about re-biopsy after a negative result is suggested to provide.

We have applied the suggested modification.

Comment 5: In the conclusion, “CT-guided FNA of pulmonary nodules is a well-established, safe, and highly useful diagnostic test” was mentioned, but the theme of the article was “CT-guided biopsy”, not “CT-guided FNA”. The conclusion should be more closely related to the title and should refer to “Radiologist’s role.”

We have applied the suggested modification.